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HEALTH, BIOECOLOGY and NANOMEDICINE

Edited by Nadiya Skotna, Svitlana Voloshanska,
Taras Kavetskyy, Aziz Eftekhari, Rovshan Khalilov

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This research work belongs to a group of authors, contains an in-depth study of the health preservation problem and the use of biosensors for this purpose, fixes the scientific priority, provides society with the primary scientific information on health promotion, the formation of environmental responsibility.

The monograph is intended primarily for scientists and meets by its content and form of publication, but will be interesting for a wide range of public. The clarity of the wording and presentation of the material, the logic of coverage for the basic ideas and concepts in it are of particular importance. Requirements to the essence of the presentation of the material in the sections of the monograph, similar to the requirements of other scientific publications with certain features of their purpose. Moreover, the issues raised in this monograph are still the subject of lively discussion among contemporary domestic and foreign scholars.

We will be glad if the monograph will not leave you indifferent and you will want to share your impressions of it.

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P R E F A C E

Nanobiotechnology is one of the 21st century's most promising technologies and there is a rising attention in the world in the development of new highly specific approaches in the diagnostic and therapeutic applications of nanobiotechnology. This field is the multidisciplinary science and carrying the science of about incomprehensibly small and portable devices closer to reality. Among different applications of nanobiotechnology in health sciences, nano pharmaceuticals, gene therapy, regenerative medicine, targeted drug delivery and disease diagnostics are the most importants. It explores the application of nanotechnology on development of safe, effective and reliable tools to combat against various infections. In the field of dentistry, the future of nanobiotechnology is very bright and facilitate precise and selective occlusion within minutes and will ensure improved oral health. Nanodentistry could also prove outstanding milestone. Nanobiotechnology holds enormous potential in the diagnosis, treatment and prevention of COVID-19 via different approaches including prohibiting viral contamination, design of infectionsafe personal protective equipment for healthcare workers and development of active antiviral disinfectants, design of highly specific/sensitive nanobiosensors to rapidly identify, improvement of new pharmaceuticals, and vaccines to boost humoral and cellular immune responses. Recently, numerous efforts have been made to improve assays for diagnosis and treatment of cancer in terms of selectivity and sensitivity based on nanobiotechnology. These developments will increase the survival rate of cancer patients by enabling early detection. Although only a few nanobotechnology-based assays have introduced to clinical trials, these methods of cancer diagnosis are poised to move into the clinic in the near future. The salient features of nanobiotechnlogical methods contribute to the degradation of waste and toxic pollutants by the action of microorganisms and plants. Bioremediation methods are different and have proven operative in restoring locations with different types of pollutants. Nano/biosensors with a bioelement (biorecognition unit) and a physical transducer (signal converting unit) have been successfully used for enhancement of functional properties of the enzymatic sensors. Nanosized materials have unique characteristics: a high sorption capacity, ability of self-assembly and, in some cases, unique catalytic properties. The integration of nanobiotechnologies seems to be very promising in further development and production of such biosensors due to the distinctive combination of chemical inertness, surface chemistry, size- and shape-dependent electronic and optical properties. The main focus of the monograph is dedicated to Concepts, applications and Perspectives combines contributions from analytical, bioorganic, and bioinorganic chemistry, physics, molecular and cell biology, and materials science in an attempt to give the reader a feel for the full scope of current and potential future developments. The articles in this volume clearly emphasize the high degree of interdisciplinary research that forms the backbone of this joint-venture of biotechnology and nanoscience. The book is divided into 3 main sections. The first concerns nanobiotechnology for human health including biofilms, dental health, kidney disease, COVID-19 and cancer. The second section is devoted biomedical and environmental aspects. Individual chapters concern the use of nanobiotechnology, such as ecological role of aquatic macrophytic vegetation and its importance to humans, Method tissue culture for obtaining of personal care products/cosmetics with extracts of plants on European standards, and Analysis of the adsorbents use for local reduction of toxic load with heavy metals. Possibility of use functional drinks based on microbiotes. And biologically active additives for the prevention of the respiratory diseases are described in the chapters on nanobiotechnoogical methods. Contributions concerning

the hydrochemical indicators and possibilities of migration of the surface water pollution of the striy district of Lviv region and the current state of medicinal plants in Ivano-Frankivsk region and their use for medicinal purposes implemented in nanobiotechnology. 6 Also, in this section deals with the areas of Kirlianography of bioelectric properties in plants and biochemical indices of blood at heart diseases of population of regions located at different altitudes. In the third section, educational aspects of ecology and human health are described beginning with study of students' adaptation to educational activity in the establishments of higher education, and Social and health preservation education sector of primary school through the prism of analysis of modern educational documents. Social aspects in patients with temporary colostoma also possess an important place in the presented monograph. We hope that the results of the theoretical, methodological and practical studies presented in the proposed collective work of the authors will be interesting both for specialists and for the general public.

Chapter 1. Rationale for the use of non-traditional treatments in patients with back pain complicated by disc herniation

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Abstract. *According to an epidemiological study of pain syndromes conducted in 19 European countries, 40% of out of more than 23,000 respondents reported back or neck pain and 21% reported foot or leg pain. In 2018 the Lancet Working Group on Low Back Pain identified a global problem of improper treatment of low back pain. For patients with low back pain, all six major international clinical guidelines preferred non-medical approaches to treatment. CareTrack study in 2019 showed that 28% of medical care for low back pain in Australia and the United States contradicted the clinical guidelines. Taking into account that with the compression of segmental structures there is a violation of venous outflow, paresis of small and big vessels, edema, sludge-shaped elements, microthrombosis, which also provoking decrease in the number of functioning capillaries; that is also true for the peripheral nervous system lesions caused by viral infections, especially coronavirus infection. In our work we during the we used non-traditional, pathogenetically determined methods of treatment in patients with back pain complicated by intervertebral disc herniation. We are considering it expedient to carry out conservative treatment by methods of manual therapy, reflexology (including acupuncture, Lyapko applicators, acupressure), ozone therapy, vacuum therapy, physiotherapy, in particular percutaneous electrical stimulation with acupuncture, kinesitherapy.*

Key words**:** *back pain, coronavirus infection, manual therapy, acupuncture, ozone therapy, percutaneous electrical stimulation, acupressure, vacuum therapy, Lyapko application devices, kinesitherapy.*

Introduction

In Ukraine, back pain (degenerative-dystrophic diseases of the spine) numbers vary up to 144.3 per 10k population, disability due to degenerative-dystrophic pathology of the spine - up to 3.1 per 10k population. The proportion of patients with degenerative-dystrophic diseases reaches more than 80% of all patients with spinal pathology and more than 30% in neurological departments (Babinets, & Nadkevich, 2019).

According to an epidemiological study of pain syndromes conducted in 19 European countries, out of more than 23,000 respondents, 40% reported back or neck pain, 21% reported foot or leg pain, and 22% suffered hand or arm pain (Todd, McNamara, & Balaj, 2019).

In recent years, the attention of not only doctors but also the population to non-traditional methods of treatment has increased both in Ukraine and abroad.

At the beginning of the XXI century, a written survey was conducted among 10,000 residents of the United States, Britain and Israel on the topic "Have you resorted to alternative medicine or non-drug treatments if you still haven't recovered?". More than 55% (5646) of people gave a positive answer. The second question concerned which method the respondents gave greater preference. The answers were distributed as follows:

30% – used herbal medicine,

20% – used homeopathy,

15% – acupuncture and cauterization,

13% – used manual therapy,

8% – used hypnotherapy,

7% – meditation and relaxation,

2% – used the services of a masseur,

2% – used aromatherapy (Dovgyi, Sereda, & Khanenko, 2007).

A survey of nearly 200,000 people in 43 countries found that patients with back pain were almost twice as likely to have one in five mental health disorders (depression, anxiety, stress, psychosis and insomnia) compared to people without back pain (Mendelevich, 2019). Pain and depression are also independently associated with chronic fatigue syndrome. The prevalence of chronic fatigue syndrome reached up to 70% in patients with chronic low back pain (up to 40% according to our data). Similarly, patients with chronic fatigue syndrome report a higher intensity of pain, depressive symptoms and a higher risk of disability (Snekkevik, Eriksen, Tangen, Chalder, & Reme, 2014).

It is important to consider the risk factors that increase stress: hypoxia, hypothermia, overheating and noise. Musculoskeletal pain is more common during cold work. Symptoms increase with people in a cold environment for a longer period of time (Pienimäki, 2002; Pienimäki, Karppinen, Rintamäki, & Borodulin, 2012; Mannekens, 2016). That is, staying or working in the cold may increase the risk of back pain (Burström, Järvholm, Nilsson, & Wahlström, 2013). According to our data, cold lesions (acute or chronic hypothermia) of patients come across in 22-30% of cases. The calf muscle is considered the most vulnerable part of the leg, as it is often exposed to hypothermia, overexertion, radiating pain in vertebrogenic pathology, especially of discogenic origin. Hypothermia, which is not an etiological factor, causes circulatory disorders in the root area, and in pre-existing vertebrogenic pathology can cause exacerbation of discoradicular conflict (Dovgyi, 2016).

We currently have the assumption that local hypothermia of the muscles of the extremities may play an etiological role in the occurrence of pelvic pathology and lower back pain due to the

physical transfer of cooler blood from the lower extremities to the pelvic plexus, where cold spasm can cause blood circulation to get disturbed, creating conditions for the pathology development (research is still being conducted).

CareTrack studies have shown that 28% of low back pain care in Australia (based on 164 patients) and in the United States (based on 489 patients) comes contrary to clinical guidelines (Traeger, Buchbinder, & Elshaug, 2019). In 2018, the Lancet Working Group on Low Back Pain identified the global problem of improper treatment of low back pain. In particular, for patients with low back pain, all six major international clinical guidelines have given priority to non-medical approaches to treatment (Qaseem, Wilt, & McLean, 2017; Chenot, Greitemann, & Kladny, 2017; Stochkendahl, Kjaer, & Hartvigsen, 2018). Decreasing role of medical treatment for low back pain is reflected in recent clinical guidelines (Hartvigsen, & Hancock, 2018; Foster, Anema, Buchbinder R, & v. Tulder, 2018). For patients at risk of developing chronic pain and disability, experts are considering the possibility of offering procedures such as spine manipulation, massage, acupuncture, yoga, psychological therapy or multidisciplinary rehabilitation (Traeger, Buchbinder, & Elshaug, 2019).

It's essential to remember that the peripheral nervous system is one integral system with the central nervous system (CNS) and interacts closely with it. It connects the CNS with all organs and tissues of the body, not only by conducting nerve impulses, but also by transferring macromolecules between the CNS and internal organs. The amount of intracellular potassium and sodium, which balance is maintained by the sodium pump, determines the electrical activity of cell membranes. The electrical activity of cell membranes is regulated by opening or closing the potential-dependent sodium and potassium channels located near the Ranvier constrictions. Axon's greatest energy needs are concetrated in the Ranvier constriction zone, where glucose is broken down aerobically (Dovgyi, 2016). This once again confirms the feasibility of acupuncture, percutaneous electrical nerve stimulation (PENS) and ozone therapy.

Myelin does not cover the nerve fiber completely, but intermittently at regular intervals (Ranvier interceptions). Between these gaps in the myelin sheath lay small gaps – so-called Schmidt-Lanterman notches. These are places where the formation of myelin cytoplasm is delayed due to circular twisting of the Schwann cell around the nerve fiber (Macheret, Dovgyi, & Korkushko, 2006). Actually Schwann cells make up a myelin cover and have length from 100 microns to 1 mm (Silantyev, 2006). In the case of microcirculation insufficiency, there are violations of venous outflow and increased pressure, in particular in the spinal plexuses (Dovgyi, 2016).

In general, the conduction of impulses is based on the electrical properties of excitability and conductivity, which are inherent in all electroexcitable tissues: nerve, muscle and glandular tissue. This is also one of the main functions of the neuron. Its membrane has an electric charge with a negative potential (more precisely, a resting potential) on the inner surface and a positive one on the outer surface. The resting potential, actively maintained by the cell, is from 50 to 90 mV. The potential is formed due to the redistribution of sodium and potassium ions. The cytoplasm of the neuron (compared to extracellular fluid) contains 10 times less sodium ions, up to 50 times more potassium ions and 50 times less chlorine ions. Irritation of the membrane by stimuli (chemical, mechanical, electrical) causes a change in ion concentrations: significantly increases the permeability of the membrane for the passage of sodium ions into the cell and to a lesser extent – for the flow of potassium ions in the opposite direction. In this process, the membrane depolarizes

and the action potential is formed. The development of action potential occurs on the all-or-none principle (Belyakov, & Gustov, 2007).

The diameter of nerve fibers varies from 1.0–2.0 to 8.0–20.0 μm, depending on the degree of their myelination. Most peripheral nerves perform mixed functions, so they are composed of motor, sensory and autonomic fibers close together (Macheret, Dovgyi, & Korkushko, 2006). This explains the simultaneous occurrence of sensitive, motor and autonomic manifestations in case of nerve damage. However, more or less isolated disorders can occur with a selective lesion of a particular type of fiber.

Spinal nerves and their roots, compared to peripheral nerves, are covered with thin epineurium and perineurium with limited resistance to chemical and dyscirculatory stimuli. Each nerve fiber of the spinal nerve, in turn, is "dressed" in the endoneurium, the tubules of which contain Schwann cells covering the myelin sheath of the fiber.

Thin epi- and perineuria, poorly developed connective tissue structures of the spinal canal, are an unreliable barrier to maintain the ionic balance of interstitial fluid. These biochemical abnormalities complement the mechanical factor of nerve and root damage. As a result, this set of mechanical, chemical and dyscirculatory factors can lead to radicular lesions – radiculopathies (Ulysses, 2014).

Nerves are provided with vessels with a dense network of anastomoses. The circulatory and lymphatic systems are quite important for the nervous system.

Peripheral nerves contain sensitive and motor fibers, sensitive only fibers or motor only fibers. Sensitive fibers begin with the receptors on the skin, muscles, ligaments and bones, and end at the neurons of the posterior roots. When the sensitive nerves are damaged, the sensitivity changes within the innervation zone of the peripheral nerves (decreased skin sensitivity), hyperesthesia (increased sensitivity), paresthesia (unpleasant sensations of numbness), hyperpathy (distorted sensitivity with an increased threshold of its perception). Some sensitive fibers have a myelin sheath, some don’t. As a rule, motor fibers have a developed myelin sheath. When motor fibers gets damaged, there are signs of weakness and decreased tone of certain muscles, their atrophy (with severe damage to axons). These injuries are manifested in motor disorders: fasciculations (short-term involuntary muscle contraction in the form of subcutaneous tremor), cramps (painful cramps), pseudoathetoid movements (slow involuntary violent movements due to tonic muscle contraction) and tremor (Silantiev, 2006).

Nerve dysfunction can be associated with: direct nerve damage or ischemia due to damage to its arteries (Dovgyi, 2016).

The spine is a kind of mobile "case" for the spinal cord and its roots. In the course of human life, degenerative-dystrophic changes develop in the spine structures: deforming spondylosis of the spinal longitudinal ligaments, deforming spondyloarthritis, osteochondrosis, disc fibrosis, vertebral osteoporosis, etc. At excessive loadings (or without them) on a backbone, in particular on intervertebral apertures, hernial protrusions of intervertebral disks, and is more exact extrusion, prolapse, and also protrusions, kernels of intervertebral disks can be formed.

An important point to be noted at once is that most common degenerative-dystrophic manifestations (protrusions and hernias of intervertebral discs) occur in the population of developed countries, where hypodynamia is a common finding. Asymptomatic intervertebral disc herniation is many times more common than intervertebral hernias, which cause back pain, or rather back and limb pain. Size does not matter much here (Sviridova, 2015).

Nerve roots pass through the intervertebral foramina slightly obliquely from top to bottom. In front of the roots the vertebral body is flowing into the intervertebral foramina; after leaving the intervertebral foramen, the root comes into contact with the posterolateral surface of the intervertebral disc. The nerve root, passing through the intervertebral foramen, occupies a third of the total volume. The rest of the hole is occupied by blood vessels, connective tissue, receptor nerves of the spine and spinal nerve. Thus, the intervertebral foramen is filled with following: nerve root, sinuvertebral nerve, artery, root vein, intervertebral veins. Actually, first of all, various mechanical or chemical processes have their influence on the veins (Fig. 1). Therefore, we believe that the appropriate tactics of pathogenetic treatment shall take into account these data (Dovgyi, 2016).

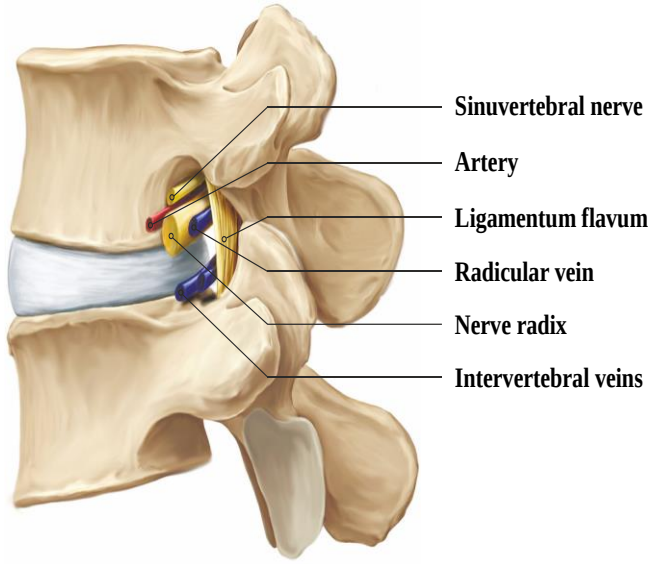

Fig. 1. Location of veins, arteries, nerves in the intervertebral foramen (Dovgyi, 2016).

The spine has at least four functions: supporting, protective, cushioning and motor. It is a flexible rod: a support for the head, shoulder girdle and arms, thoracic and abdominal cavities, the weight of which is transferred to the pelvic girdle and legs. Due to the supporting function, the vertebrae own a different structure. The protective function of the spinal cord is to protect the spinal cord from mechanical damage. Essentially, the flexibility of the spine stays of great importance for the absorption of shocks and concussions, protecting the brain from trauma to the bone structure of the skull. Muscles, intervertebral discs, joint fissures, and vertebral joint surfaces are involved in cushioning. The presence of physiological curvature (cervical and lumbar lordosis) also plays a significant role here. Motor function is performed in the intervertebral joints around three axes: frontal, sagittal and vertical. There are passive part (vertebrae, joints, ligaments, discs) and active – the muscular system (Dovgyi, 2016). Muscles have vessels (arteries, veins) that can contract due to prolonged spasm of the same muscles. Prolonged vascular compression creates the conditions for the development of hypoxia in the so-called transitional areas with fewer functioning capillaries and, accordingly, poorer collateral blood flow (Kolisnyk, 2019).

We live in a three-dimensional world in which it is quite difficult to find motion occuring in one plane only. In wildlife it is almost impossible. And the vertebra therefore can and do move in all three planes.

The largest number of joints is located in the spine, reaching about a hundred. Former WHO Director-General G. Brundtland (doctor, former Prime Minister of Norway) said that diseases of the bones and joints make the main cause of persistent pain and physical deterioration.

Joints provide mobility of the musculoskeletal system. Functionally and clinically, joints are inseparable from muscles, ligaments, and the nervous system that controls movement. 70% of the information conducted to the brain is analyzed at the lower levels of the nervous system and only 30% reaches the cerebral cortex. At the same time, every muscle, even the smallest, owns its representation in the cerebral cortex (Sitel, 2008; Dovgyi, 2016).

The pathology of the spine and changes in the segments lead to dysfunction of the relevant organs, which are connected through the autonomic structures. The nature of microhemodynamic changes depends on the type of pathological autonomic impulse from the segments. Irritation of segmental sympathetic vegetative structures leads to excessive impulses, which causes spasms of arterioles and lower number of functioning capillaries. With a decrease in the intensity of autonomic impulses or impulses' blockade during compression of segmental structures paresis of microvessels, edema, sludge of shaped elements, microthrombosis occures, which also drops the number of functioning capillaries (Kolisnyk, 2002; Kolisnyk, 2019). It is important that the veins collect blood from the capillary bed through the anastomosing postcapillary venules. Increased vascular permeability is characteristic of inflammation (edema), observed in postcapillary venules (Kumar, 2019).

With the development of pathological changes in the shape of the spine the preconditions for dystopia, ie displacement of internal organs take place, leading to deformation of arteries, veins, lymphatic vessels involved in blood and lymph supply of organs, as well as excretory ducts, causing disruption of arterial, and most importantly venous and lymphatic outflow, violation of the evacuation of secretions (urine, bile, pancreatic juice etc.) (Kolisnyk, 2019).

The human spine goes through an individual path of development, which depends on certain living conditions. The concept of "living conditions" includes physical, psychological and emotional stress, disease, food quality, environmental conditions. And the "environmental conditions" that dramatically affect the development of the spine: the influence of gravitational forces, changes in atmospheric pressure, electromagnetic balance, thermal regime, ionizing radiation, and others. Transformations of the morphology of the skeleton and spine usually occur with an interval of 7 years (Tonkov, 1946; Orel, 2010).

The human body has a separate, as yet insufficiently studied, functional system of regulation of electromagnetic balance (system of electromagnetic homeostasis). It controls all the vital processes, ensures optimal performance of vital functions through close interaction with other known control systems (nervous, endocrine, immune). The system of electromagnetic homeostasis is represented by the corresponding structures at purely molecular, cellular, tissue levels. It is believed that the role of electromagnetoreceptors at the molecular and cellular level is performed by water and collagen molecules, and at the tissue level with the acupuncture points and the channel-meridian system (Golub, Koptelov, & Bondar, 2018). We are studying the system of electromagnetic homeostasis using a device for monitoring the spectral-dynamic parameters (KSD), in particular for acupuncture diagnosis and subsequently for more effective treatment.

As an result, the spine of each person (although, perhaps, relatively) can be called unique. This should be considered when examining the patient, for examination, differential diagnosis and subsequent treatment tactics.

Analysis of recent research

First of all, patients with discogenic lesions of the nervous system in the acute period should be recommended for the appointment of the most gentle motor and physical regime to stay in a semi-hard bed. The duration of bed rest is not more than 2-3 days. After that, it is advised to gradually expand motor activity and therapeutic exercises to reduce the likelihood of developing chronic pain.

General principles of drug therapy of vertebrogenic pathology are aimed at the purchase or control of pain - nonsteroidal anti-inflammatory drugs, analgesics, antidepressants, improving regional blood and lymph circulation, microcirculation and tissue trophism – euphylline, nicotinic acid, No-spa, vectocontal, trentonal, trentonal euphyllin, detralex, as well as lasix, vitamins B, C, E, biogenic stimulants, including plasmol (Klimenko, Golovchenko, & Kalischuk-Slobodin, 2008; Dovgyi, 2016; Kozolkin, Medvedkova, & Revenko, 2020).

To eliminate the pain syndrome, various methods of reflexology are widely used: acupuncture, electrocupuncture, especially acupressure, micro-acupuncture, auriculopuncture, stimulation with a beam of needles. It is necessary to take into account the genesis of pain syndromes, the topic of the lesion (including muscular-tonic, vegetative-vascular and neurodystrophic manifestations, pathogenetic features of the pain syndrome, course and stage of the disease, degree of functional disorders), number of trigger points, presence of visceral pathology. when acupuncture is rather effective (Dovgyi, 2016; Kozolkin, Medvedkova, & Revenko, 2020). Superficial multi-needle therapy use Lyapko applicator devices (Lyapko, Dzhuzha, & Lyapko-Arshinova, 2009; Dovgyi, 2016).

Manual therapy (MT) is used to eliminate functional disorders of joints and muscles and to treat pain syndrome. For the treatment of vertebrogenic pathology of discogenic genesis, following classical MT methods are used: postisometric relaxation, mobilization, manipulation (Dovgyi, 2016; Traeger, Buchbinder, & Elshaug, 2019; Kozolkin, Medvedkova, & Revenko, 2020; Taran, 2021).

Ozone therapy is used to restore microcirculation and improve tissue trophism. In addition to the vasodilating effect, ozone therapy improves tissue oxygen supply, reduces tissue hypoxia, including tumor processes, activates gas exchange in the area of ischemia, improves peripheral blood circulation, facilitates venous outflow from the extremities, reduces tissue edema, 2003; Shmakova, Nazarov, Barkhotkina, & Ivanov, 2014; Dovgyi, 2016; Andryushchenko, 2019; Schwartz A, 2021). This is quite relevant given the postcocious syndrome, in particular the effects on blood vessels, especially veins, and increased immunity.

Among physiotherapeutic methods we prefer phonophoresis or electrophoresis with solutions of analgesic drugs, sinusoidal modulated currents, pulse currents of low frequency, in particular amplipulse therapy, diadynamic current; quite effective percutaneous electrical nerve stimulation (PENS). The complex of physiotherapeutic treatment also includes magnetic therapy, which performs the function of the basic method of long-term action. Drug medical blockades (DMB) are used to treat pain syndrome (with ozonated air or anesthetic), ie carrying the substance to the site of the pathological focus causing the pain (Dovgyi, 2016).

We also carry out kinesitherapy in order to strengthen the "muscular corset", following the main rules, including increasing the dose of exercise during the procedure and course (with a maximum load in the middle of the procedure) with repetition of each exercise 4-6 times (Kozolkin, Medvedkova, & Revenko, 2020).

Also, in addition to the above methods of treatment, patients at risk of developing chronic pain and disability, domestic and foreign clinicians, depending on what clinical recommendations they have followed, consider offering procedures such as massage, yoga, psychological therapy or multidisciplinary rehabilitation (Dovgyi, 2016; Traeger, Buchbinder, & Elshaug, 2019).

Various methods of reflexology are widely used to eliminate back pain: acupuncture, especially in combination with PENS, micro-acupuncture, auriculopuncture, irritation with a beam of needles (Lyapko rollers), especially acupressure. Considering the pathogenetic genesis of pain vertebrogenic syndromes, the topic of lesions (local and distant manifestations, the presence of vertebral syndrome, muscular-tonic, vascular and neurodystrophic manifestations, pathogenetic features of pain, course and stage of disease, degree of pathological presence, degree of pathology) stays essential. (Dovgyi, 2016; Sviridova, & Morozova, 2017). Superficial multi-needle therapy uses Lyapko applicator devices (Lyapko, Dzhuzha, & Lyapko-Arshinova, 2009; Dovgyi, 2016).

One of the reasons for carring out kinesitherapy is to strengthen the "muscular corset", following the main rules, as increasing the dose of exercise during the procedure and course (with the maximum load in the middle of the procedure) with repetition of each exercise 4-6 times (Kozolkin, Medvedkova, & Revenko, 2020).

The purpose of the study: to use clinical-neurological, instrumental, laboratory methods to improve the understanding of the state of functional activity of the vascular system in vertebrogenic pathology, and to determine approaches to improving the algorithm of treatment of patients. We use magnetic resonance imaging (MRI), radiography with functional tests, capillaroscopy, duplex ultrasonographic scanning of arteries and veins of the lower extremities, device controlling spectral and dynamic characteristics of a human being (KSD), tests (visual-analog scale (VAS), McGill pain questionnaire, DN4 questionnaire, Hamilton depression rating scale) to clarify the pathogenetic mechanisms of the disease.

Material and methods of the research

On the basis of the Department of Neurology and Reflexology of the National University of Health of Ukraine named after P.L. Shupyk ("Doctor Dovgyi Clinic") we examined and treated 28 patients, 16 female (57.2%), 12 male (42.8%), age range 20 to 68 years. Duration of exacerbation of the disease from 1 week to 6 months.

The diagnosis was confirmed by MRI, lumbosacral radiography in two projections with functional tests, capillaroscopy, duplex ultrasonographic scanning of the vessels of the lower extremities, SDP, appropriate tests.

The patient's age, leading pathogenetic genesis of pain vertebrogenic syndromes, variants of the clinical picture of the neurological syndrome, somatic status, duration and stage of the disease are important in the treatment.

Results of the research and their discussion

Individual, consistent, pathogenetically conditioned treatment by methods of manual therapy, reflexology, including acupressure, vacuum therapy, physiotherapy, kinesitherapy and other non-drug methods was used.

MT techniques were chosen taking into account the characteristics of symptoms, including neurological, the severity of pain, the degree of tension in the muscles, the location of the hernia or protrusion of the intervertebral disc.

Before performing MT, segmental or acupressure massage was performed to relieve muscle spasm and reduce their tension. Acupressure has been performed in patients with radicular

syndromes in combination with the Booster vibrating massager, especially to relieve gluteal hypertension on the affected side, which clinicians do not always pay attention to.

The MT session began with post-isometric relaxation techniques aimed at relaxing the muscles.

The success of manual treatment does not depend on the size of the hernia (including sequestered), but rather on the size of the vertebral canal, the condition of the muscular and especially the circulatory system, in particular the condition of the veins. This is even more relevant given the post-COVID syndrome.

We used classical acupuncture in the first one or two sessions used tonic acupuncture points (AP) and local points, pain points. Subsequently, the acupuncture procedure was selected individually, taking into account the patient's condition: both local-segmental and remote AP were used simultaneously. The most commonly used AP on the meridian of the bladder V 22–28, 31–34, 46–50, 60–67; as well as T 3-5, located in the zone of innervation of the respective roots.

Lyapko applicator devices were used locally in the lumbosacral region and partially in the lower thoracic region. Needle elastic Lyapko bands used in patients with pain in the leg during the innervation of the nerve, wrapping them around the corresponding lower limb; course of treatment included 4-8 and more procedures. Also 4 (14.3%) patients who had post coronavirus syndrome used Lyapko applicator suit, during the use of which the body creates a positive training stress to increase immunity.

Ozone therapy was administered as intravenous injections 8 times a day, in case of severe pain we used the paravertebral blockade with ozonated air. The purpose of ozone therapy is to restore microcirculation and improve tissue trophism.

Kinesiotherapy was usually prescribed after 3-5 sessions, taking into account the pain syndrome, mobility in the vertebromotor segment, the state of the muscular system, weather conditions.

Vacuum therapy and jar massage with ozonated oil were used topically in the lumbosacral region and, in the case of radicular syndrome, along the corresponding root to improve venous outflow, local blood and lymph circulation.

If necessary, hirudotherapy was used to improve microcirculatory disorders, eliminate ischemia and tissue hypoxia, spasm of deep paravertebral muscles, as well as restore cerebrospinal fluid dynamics, treat aseptic inflammation.

8 (28.5%) patients were offered to wear a medium fixation corset with six ribs for 3-4 months to ensure the unloading of the affected spine.

Patients were offered infusions and decoctions used for pain in the lumbar spine, as infusion of horse chestnut, burdock, Adam's root, lilac, fresh lovage shoots, decoction of birch buds, burdock compress, grated horseradish with potatoes or radish.

Aromatherapy was used with playing melodies of calm rhythm. Various essential oils were used, including lavender, mint, rosemary, eucalyptus and pine.

Evaluation of treatment results was performed according to the regression of leading clinical symptoms (elimination of pain and sensory disorders, recovery of the muscular system), assessment of clinical and neurological status, MRI data, capillaroscopy, duplex ultrasonographic scanning of lower extremities, KSD, tests (visual-analog scale (VAS), McGill's pain questionnaire, DN4 questionnaire, Hamilton's depression scale).

Significant improvement was noted in 10 (35.7%) patients, improvement in 12 (42.8%), slight improvement in 4 (14.3%) and no improvement in 2 (7.1%) (Fig. 2).

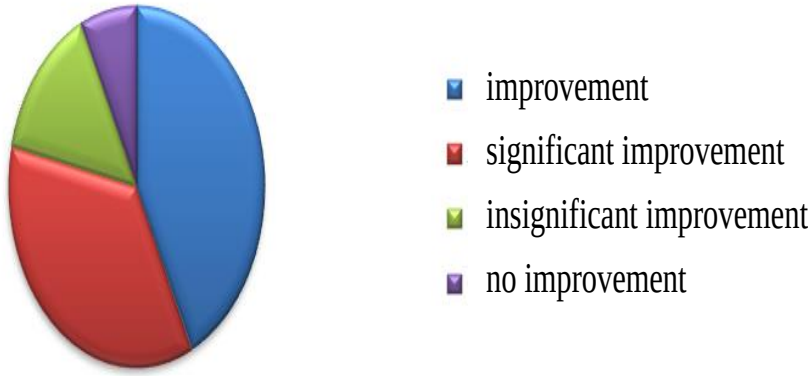

Fig. 2. State dynamics

Conclusions

We analyzed use of non-traditional methods of treatment in patients with back pain complicated by hernias, their pathogenesis, conservative treatment. We consider it expedient to carry out conservative treatment individually, pathogenetically due to the methods of manual therapy, reflexology, including acupressure, ozone therapy, vacuum therapy, physiotherapy, kinesitherapy.

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CHAPTER 2. INFLUENCE OF CHROME CITRATE NANOPARTICLES ON GROWTH AND PROLIFERATIVE ACTIVITY OF *ALLIUM CEPA L.* AS A TEST-OBJECT

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Abstract. *The biological influence of the different chrome citrate nanoparticles (CCNP) concentrations on growth and proliferative activity of Allium cepa L. as test-object are investigated. It was found that aqua CCNP solutions in the range at concentrations of 0.25–2.50 mg/l do not cause phytotoxic effects: do not change the turgescence, color and shape of the test object bulbs roots; growth activity of its roots is at the level of control, and phytotolerance is high (94.64–98.57 %). CCNP at concentrations of 5 mg/l–7.5 mg/l and above cause phytotoxic effects of high and maximum levels. It is shown that CCNP in the range at concentrations of 0.25–2.50 mg/l do not have a cytotoxic and mitosis modifying effect on the proliferative activity of cells apical meristem of the test object roots: mitotic and phase indices are within normal limits; indices of cytotoxicity are within background values. The Allium-test confirm the possibility of using CCNP in technologies of growing crops in the range of biologically acceptable concentrations (0.01-0.05 mg/l), which do not reveal any manifestations of phyto-, mito- and cytotoxicity.*

***Keywords*:** *chrome citrate nanoparticles, phytotoxicity, cytotoxicity, Allium cepa L.*

Introduction

Intensive research is conducted in recent years in nanotechnology, nanomedicine, nanothermodynamics, nanoelectronics, etc. to obtain new, more efficient, and environmentally friendly nanocompounds and nanopreparations based on them. All this became possible due to the development of new technologies to synthesize substances in the nanoscale range (Viana, 2014; Huynh, 2020).

Different types of nanoparticles have already synthesized using nanotechnology methods (Viana, 2014). Among them, essential biometals nanocitrates (EBNC), which are a product of the synthesis of new technologies of Ukrainian researchers, obtained by the erosion-explosive method, which is based on a unique physical effect in the field of high energy concentration (Kosinov, 2009). The developers of this method of nanoparticles synthesis are positioned EBNC as a source of biologically available elements important for the plants (Huliaieva, 2018) and animal biogenesis (Zakharchenko, 2017).

It is believed that nanoparticles of citrates of essential elements are environmentally safe, non-toxic, biologically susceptible and functionally bioactive. In the form of carboxylates (citrates) of organic acids, when entering the cells directly enter the Krebs cycle - one of the leading energy exchanges of cells and organisms (Kosinov, 2009; Zakharchenko, 2017; Huliaieva, 2018). It is proposed to use environmentally friendly complex micro fertilizer “Super-Eco” in crop production and horticulture (Kosinov, 2010), which contains carboxylates of trace elements in

specific quantities, including nanoparticles of chrome citrate. The developers declared that these microfertilizers is safe and environmentally friendly, as their components are carboxylates of trace elements obtained by erosion-explosive nanotechnology based on nano- and microparticles of these trace elements, their oxides and their hydroxides ranging in size from 1 nm to 15 μm.

The biological effects and toxicological properties of chrome citrate nanoparticles (CCNP) obtained by erosion-explosive nanotechnology according to the Kaplunenko-Kosinov method have not been sufficiently studied concerning plants of different cultures. Since chrome has positive and adverse effects on plant organisms depending on the state of valence and form of existence in complex compounds, it is important to determine the biological impact of chrome citrate nanoparticles. In this work, we conducted a set of studies on the effects of this is newly synthesized substance using the recommended test system and *Allium cep*a as test object (Viana, 2014; Andrusyshina, 2011).

Analysis of recent publications

Nanoparticles attract the special attention of researchers and specialists in various scientific fields due to their new and unique properties, which are different from the properties of particles in the macroscale of similar composition (Viana, 2014; Huynh, 2020; Tripathi, 2017). The passes of substances to nanometer-scale particles caused a change in their structure, physicochemical and biological properties. Such changes are large specific surface area, small size and variety of shapes, increase in chemical potential of the substance, high adsorption activity, high ability to accumulate. Some metal nanoparticles have biocidal, electrical, catalytic and magnetic properties, which is the basis of their classification (Viana, 2014). Studies of the physicochemical properties of a wide range of nanoparticles show that they are the functions of many known and unknown interrelated parameters: technology, time, environment, shape, size and size distribution curve in the nanoscale range, chemical purity, the presence of electrical matter on the surface charge, presence and composition of the stabilizing shell and others (Viana, 2014; Huynh, 2020).

Modern society has already benefited significantly from nanotechnology, as many products with improved properties and a high potential for use have been synthesized and commercialized (Bijali, 2020; Fincheira, 2020). In particular, nanoparticles of different chemical compositions are already used in the detection of toxins and pathogens, diagnosis and treatment of diseases, drug delivery to target organs and cells, product bio labeling, biological and chemical analysis, visualization of results in nonlinear optics, photovoltaics, catalysis, and others. Nanometals are used during the creation of new effective catalysts for the petrochemical industry, for the manufacture of modern sensor systems, in the diagnosis and treatment of infectious and oncological diseases, obtaining materials with bactericidal action, to create new drugs for protection and growth of plants and animals in agriculture and veterinary medicine, in environmental protection (Fakruddin, 2012).

The use of nanopreparation for agriculture is promising (Zhao; 13; Yadav, 2014; Fincheira, 2020), especially of nanoparticles containing essential metals that can be an alternative to mineral fertilizers (Andrusyshina, 2011; Fincheira, 2020). It turned out that some of the applied nanocompounds are important biological regulators of morphogenetic processes in plants. Their role in the processes of growth, differentiation, restoration and regeneration, apoptosis, necrosis, cell survival, and the pathogenesis of chronic inflammatory and degenerative diseases of animals and humans has been proven (Jitao, 2019). It is proved that the lack of trace elements not only leads to lower yields and the development of some diseases in plants and animals but also reduces the quality of food (Arruda, 2015). Studies have shown that some human diseases are associated with a lack of iron, zinc, copper, cobalt, molybdenum, iodine, etc., in food (Jitao, 2019). Therefore, the problem of providing plants and animals with trace elements is of general biological importance.

The active development of nanotechnologies and the introduction of nanoproducts in various sectors of the economy, on the other hand, is of concern to the scientific community about their environmental friendliness and possible toxicity to environmental ecosystems (Andrusyshina, 2011; Yadav, 2014; Fincheira P., 2020). Several studies have shown that some nanoscale particles

sometimes exhibit specific toxicity and may be more harmful than substances of the macroscale (Tripathi, 2017). The accumulation of nanoparticles and nanomaterials in the environment can be hazardous because of the potential harm to plants and because they can enter the food chains (Yadav, 2014). Although the scientific literature on the safety of nanoproducts is growing, the mechanisms by which these materials cause toxicity to natural species, including humans, have not yet been definitively elucidated. There is experimental evidence that nanoparticles such as fullerenes, carbon nanotubes, and metal oxides are toxic to human cells, rodents, and microorganisms (Andrusyshina, 2011; Ivask, 2013). Data on the potential toxicity of nanoparticles to higher plants vary (Yadav, 2014), both positive and negative influences have been reported in the scientific literature (Tripathi, 2017). The interaction between nanoparticles and plants is one of the fundamental problems due to the active introduction of nanoparticles and nanomaterials in the technology of growing crops, long-term storage of agricultural products (Zhao, 2020).

Among biota, plants are suitable for studying the effects of nanoparticles and nanomaterials because they are sensitive to their impact (Tripathi, 2017; Huliaieva H., 2018). It is noted that nanoparticles have several effects on plant physiology and morphology, in particular, on root structure, seed germination, and cellular metabolism (Ivask, 2013; Tripathi, 2017). Some of the nanoparticles inhibit growth, induce oxidative stress, morphogenetic abnormalities and cause clastogenic disorders in some plant species (Huliaieva H., 2018). The size, shape, and surface coating of nanoparticles and nanomaterials have been shown to play an essential role in determining their level of phytotoxicity. Dose, route of administration, type of dispersion medium, and environmental exposure are also essential factors in the formation of phytotoxicity of nanoparticles (Huliaieva H., 2018; Zhao, 2020).

Analysis of work on the phytotoxicity of different nanoparticles and nanomaterials on different plant species shows that the results of their studies are very different (Ivask, 2013; Huliaieva H., 2018; Zhao, 2020). This may be due to the different reactions of the plant depending on their species and the nature and mechanism of action of the studied nanocompound. Before that, most studies to date have focused on the microscopic detection of phytotoxic effects of nanoparticles. Obviously, additional research is needed, including methods and analyzes made using more modern tools (Zhao, 2020).

For a comprehensive study of the toxicity of nanoparticles of various natures, some plant species began to be used as test objects. The mechanisms of toxicity for different types of nanoparticles on plant systems, their absorption mechanisms, distribution in tissues and organs, and subsequent migration on food chains have been studied within this direction (Zhao, 2020). In the works of various authors, recommendations, methods, and methods for assessing the phytotoxicity of nanoparticles by morphoanatomical, physiological, biochemical, and molecular characteristics of plants (Huliaieva, 2018; Ivask, 2013; Yadav T., 2014; Tripathi, 2017). In particular, the phytotoxic effect of Argentum and zinc oxide nanoparticles on *Allium cepa* onion and *Zea mays* corn, *Cucumis sativus cucumber*, and *Lycopersicum esculentum* tomatoes was established by the growth test method. Nanoparticles are also evaluated for their ability to induce cytotoxic and genotoxic effects in the apical meristem of the roots of *A. cepa* bulbs. The mitotic index, the frequency of chromosomal mutations, metaphase disturbances, ruptures, and micronuclei formation were determined in these studies (Kumari M., 2011). Phytotoxicity of dispersed nanoparticles are tested in vitro and in vivo on the seeds of some plants treated with different concentrations, in which root length, germination effect, adsorption, and accumulation of nanoparticles in plant systems were determined. Evaluation of the effect of nanoparticles on the concentration of proteins, DNA, and thiobarbituric acid was performed by biochemical studies, which analyze the functional and conformational changes of biomolecules (Tripathi, 2017). It has been found that some nanoparticles can induce or decrease the regulation of marker genes, affect the transport and retention of water, cell wall formation, and cell division (Tripathi, 2017). Several studies indicate that the phytotoxicity of nanoparticles depends on various factors: their size, shape, carrier, coating, and experimental methods (Yadav T., 2014; Ivask, 2013).

Thus, nanoparticles, depending on the physicochemical nature, can induce various changes in morpho-anatomical, physiological, biochemical, and molecular characteristics in plants. The literature data suggest that a larger number of engineered nanoparticles, although it has significant advantages in various areas and areas of human activity, which requires factual information and a science-based database on their toxicity in the use of biosafety and reduction of harmful risks during use and consumption.

Thus, the research of the influence of nanoparticles containing important elements for processes of plant morphogenesis, which are planned for use in agricultural cultures production technologies, is a relevant topic, as it is possible to determine the safety and risks of their practical application.

The purpose of the research

The study aims to explore the biological effect of different concentrations of chrome citrate nanoparticles to morphogenesis of the test object *A. cepa*.

Material and methods of the research

The object of study. CCNP were synthesized by erosion-explosive nanotechnology according to the Kaplunenko-Kosinov method (see the patent of Ukraine for a utility model No. 38391) (Kosinov, 2009).

Patent owners note that the drug does not contain other substances, and nanoparticles of essential metal are fully involved in the chemical reaction of synthesis with citric acid salts, resulting in a product of high chemical purity and, most importantly, the resulting compound does not contain free nanoparticles (Kosinov, 2009).

The drug nanoparticles of chrome citrate with a concentration of 1 g/l were used for research. Working CCNP solutions with concentrations of 0.01 to 10 mg/l were prepared by diluting the original preparation with distilled water.

Determination of phytotoxicity for chrome citrate nanopartices was performed by growth *Allium* test using a standard plant test system *A. cepa* (L.) (Fiskesjo, 1997). The phytotoxicity of chrome citrate nanoparticle solutions against *A. cepa* was determined in the concentration range of 0.01 to 10.0 mg/l with a modified variant: the test object *(A. cepa*) bulbs was placed in solutions of nanoparticles of different concentrations without prior root germination (Konotop, 2019).

Laying down the experiment. In control and experimental (at least four analytical replicates and three biological replicates), *A. cepa* bulbs of the Stuttgart variety were placed in 15-ml tubes with working CCNP solutions so that their bottom was utterly immersed. Whole, intact, identical in size (diameter 16 ± 2 mm) and weight (2.90±0.10 g) bulbs of *A. cepa* without green shoots were selected for the experiment.

Exposure of *A. cepa* bulbs in working CCNP solutions was carried out at room temperature (20±2 °C) and dark conditions for five days (to achieve roots of at least 20 mm). Distilled water served as a control.

The overall toxicity of chrome citrate nanoparticle solutions was determined by visually analyzing the turgescence, color, and shape of the germinated roots of *A. cepa* bulbs (on the fifth day of exposure) in control and experimental variants (Konotop, 2019; Lin, 2007).

The phytotoxicity of chrome citrate nanoparticle solutions was determined by growth assay (Fiskesjo, 1993). At the end of the exposure time (after five days), the length (in mm) of the sprouted roots of *A. cepa* bulbs was measured in the control and experimental variants.

The mean value (M) and its error (m) of bulb root length for each experimental (ME) and control (Mk) variants were calculated. The results were recorded in the appropriate table. The Student's test assessed the significance of the difference between the control and experimental variants.

The phytotoxicity index (IFT) of chrome citrate nanoparticle solutions, which is an indicator of the growth activity of the roots of *A. cepa* bulbs, was calculated by the formula:

$$IFT = \frac{Mk - M_E}{Mk} \times 100\%$$

where:
$IFT_{\%}$ – phytotoxicity index of the sample;
M_K – the magnitude of the test reaction in the control sample;
M_E – the value of test reactions in the test sample.

The phytotoxicity of nanoparticles was assessed on a five-point scale (Konotop, 2019) : 0 -20% – no or low level of toxicity; 20.1-40% - the average level of toxicity; 40.1–60 – above average toxicity; 60.1–80 – high level of toxicity; 80.1-100 – the maximum level of toxicity.

The formula determined the tolerance index (IT %) of the roots of the bulbs of *A. cepa* concerning solutions of nanoparticles determined by the formula (Konotop, 2019):

$$IT = \frac{Md}{Mk} \times 100\%$$

where:
M_d is the average value of the root length of the experimental variant;
M_k is the average value of the root length of the control variant.

Determination of CCNP cytotoxicity by Allium test. The cytotoxicity of a CCNP solution was understood as inhibition of cell proliferation and growth of the test object. Its indicator is the mitotic index (MI) of the cells of the meristem of the roots of the bulbs of *A. cepa* (Fiskesjo, 1997). The mitosis modifying effect of aof CCNP solution was understood as a violation of the passage of cells of the meristem of the test object of the phases of mitosis. Its indicator is the phase indices (IF) of the cells of the meristem of the roots of the bulbs of *A. cepa* (Fiskesjo, 1997).

Scheme of analysis. The tips of the roots of the bulbs of *A. cepa* experimental and control variant length of about 10-15 mm were cut off, fixed, stained, and studied microscopically.

Fixation of roots. The cut roots of A. cepa bulbs were placed in sealed containers with Clark solution (mixture of 96% ethanol and glacial acetic acid, 3v: 1v). After 3-5 hours, the material was washed with 70% ethanol and placed in a container with 70% ethanol for long-term storage.

Staining of the roots of *A. cepa* bulbs was carried out with 2% acetoorsein (2 g of orcein was dissolved by heating to secret boiling in 100 ml of 45% acetic acid and filtered). The roots of A. cepa bulbs were placed in beakers with distilled water. For washing after lowering them to the bottom of the cup, they were transferred to porcelain crucibles with dye. The crucible was covered with a glass plate, heated to a secret boil (glass fogging), and left for 2 – 24 h to stain the cells. Stained roots of *A. cepa* bulbs were used for the preparation of temporary cytological preparations.

Microscopic analysis. Temporary cyst preparations from the roots of A. cepa bulbs were prepared as follows: the meristem 2-3 mm long was cut off from the painted source with a scalpel, placed on a glass slide in a drop of 2% acetoorsein, covered with a cover glass and light tapping of the handle). Preparations of A. cepa roots were analyzed microscopically (at a magnification of 15x8 and 15x40). Cells at different stages of mitosis were visualized, photographed, and counted using a microscope attachment connected to a computer and PVR-PLUS.

Determination of mitotic and phase indexes. Mitotic index (MI%) is an indicator of cells dividing the total number of all cells. Determination of MI was performed by analyzing at least 500 cells (including interphase) meristems of the roots of *A. cepa* bulbs.

The **mitotic index** (MI%) was determined by the formula:

$$IM = \frac{(P + M + A + T)}{N} \times 100\%$$

where:
(P+M+A+T) – the sum of cells that are at the stage of pro-, meta-, ana- and telophase;
N is the total number of counted cells (including interphase).

The **phase index (IP %)** was determined by the formula:

$$IP = \frac{(FN)}{(P + M = A + T)} \times 100\ \%$$

where: $IP_{\%}$ – phase index;
FN – the number of cells at acertain stage of the mitosis phase;
(P + M + A + T) – the total number of cells at the stages of pro-, meta-, ana- and telophase.

The **cytotoxicity index (CI%)** was determined by the formula:

$$CI = \frac{IM_E - IM_K}{IM_E} \times 100\ \%$$

where :
IM_E – the average value of the mitotic index of the roots of the experimental variant;
IM_K – the average value of the mitotic index of the roots of control.

Statistical analysis of experimental data. The experiments were performed in at least three biological and four analytical replicates. For each sample, the arithmetic mean (M), standard error of the mean (m), Student's test (t), and reliability (p) were determined. The data were considered reliable at a significance level of $p \leq 0.05$.

Results of the research and their discussion

Research of phytotoxicity of CCNP by growth test.

Phytotoxicity of CCNP (in the range of concentrations 0.01–10.0 mg/l), obtained by erosion-explosive technology, was evaluated by the growth *Allium*-test (Fiskesjo, 1993; Fiskesjo, 1997).

A. cepa bulbs and seeds are widely used in tests for toxicity of test substances of synthetic or natural origin (Blinova, 2013; Lin, 2007) to detect the toxicity substances in the environment (water, soil) (Konotop, 2019; Klepach, 2001). In the *Allium*-test analyzes, the growth and mitotic activity of the roots of *A. cepa* bulbs is analysed (Fiskesjo, 1993). It is a widely recognized bioassay method for assessing the toxicity or non-toxicity of a compound, recommended by the International Commission on Protection against Mutagenic and Carcinogenic Compounds along with other methods (Guide, 1985). This method is convenient, easy to perform and gives a more objective assessment of the toxicity for test substances compared to chemical ones, especially in the case presence of upper limits of maximum permissible concentrations of substances (Guide, 1985).

In the first stage of the *Allium*-test, we observed and evaluated the growth activity of the roots of *A. cepa* bulbs during the exposure time (see *Figure 2*). In the fifth day of exposure, we conducted visual analysis of the roots of *A. cepa* bulbs (provided they reach at least 20 mm) turgescence, color, shape (swelling and bending), and their length was measured. The results of observations and measurements are shown in *Tables 1* and *2*. As can be seen from *table 1* and *table 2*, growth activity and morphological parameters of the roots of *A. cepa* bulbs grown in CCNP solutions in the concentration range from 0.01 to 0.10 mg/l, without visible morphological and structural changes (the shape of the roots is elongated and regular, they are light, the tips are slightly pigmented). However, the growth activity of the *A. cepa* bulbs grown in CCNP solutions

in the range of concentrations from 0.05 to 1.00 mg/l is reduced. In addition, there is a change in the shape of their roots: they acquire a somewhat tortuous form.

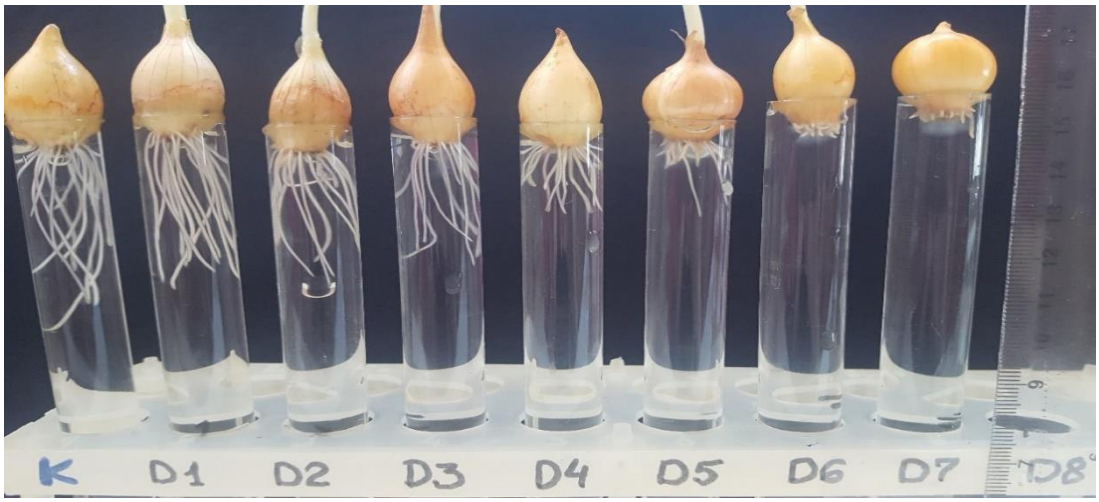

Fig. 1. Type of roots of Allium cepa bulbs on the 5th day of growth on aqueous CCNP solutions: K – control (distilled water); D1 – 0.01 mg/l; D2 – 0.05 mg/l; D3 – 0.10 mg/l; D4 – 0.50 mg/l; D5 – 1.0 mg/l; D6 – 5.0 mg/l; D7 – 10.0 mg/l.

Phytotoxicity indexes (IFT%) served to measure the phytotoxic effect of CCNP of different concentrations on the test object. IFT% is an essential indicator in the initial assessment of the impact of the test substance on the phytoobject, especially in environmental monitoring (Lin, 2007). Thus, CCNP solutions in the concentration range of 0.01–0.05 mg/l do not cause changes in turgescence, color, and shape of the tips of the roots of the bulbs of the test object (see Table 1).

Table 1

Morphological parameters of the roots of *Allium cepa* bulbs grown on aqua solutions of chrome citrate nanoparticles

Name of samples	Concentration of chrome citrate nanoparticles, mg/l	Turgescence	Shape of the roots	Color of the roots
K	Control	Normal	Elongated correct	Bright with light tips
D1	0.01			
D2	0.05			
D3	0.10			
D4	0.50	Normal	Elongated, slightly tortuous	Bright with light tips
D5	1.0	Normal	meandering	Bright with light tips
D6	5.0	There is no growth		
D7	10.0			

The growth activity of its roots does not differ significantly compared to the control and experimental variants (see Table 2). These morphometric parameters of the test object indicate that at the body level of phytotoxicity of CCNP in the range of 0.01–0.05 mg/l is not observed.

The levels of tolerance (IT%) of the roots of A. cepa bulbs to these concentrations of nanoparticles is high and is 80.84 % and 92.81 %, respectively.

As can be seen from *Tables* 1 and 2 and *Figures* 2, higher concentrations of CCNP (in the range of 0.1 to 5.0 mg/l) have higher levels of phytotoxicity (see *Figure 2*) relative to the growth activity of the roots of *A. cepa* bulbs. In particular, it was determined that CCNP in the concentration range from 0.05 to 0.10 mg/l have a phytotoxic effect of medium level, in the concentration range from 0.10 to 0.50 mg/l – above-average level, from 0, 50 to 1.00 mg/l – high level concerning *A. cepa.* In the range of nanoparticle concentrations 5–10 mg/l – the growth of the roots of *A. cepa* bulbs is almost not observed: on a dark background instead of roots, thin short root hairs are visible, which easily fall off when touched from the bottom of the bulb. Thus, concentrations of CCNP of 5 mg/l and above cause phytotoxicity of the maximum (≈100) level relative to the growth activity of the test object *A. cepa.*

As we can see (see *Table 2, Figure 2*), the tolerance of *A. cepa* bulb roots to higher concentrations of CCNP decreases accordingly. Both values – phytotoxicity of higher concentrations of nanoparticles and phytotolerance of roots of *A. cepa* bulbs are negatively correlated with each other (R = -1) (see *Figure 2, B*).

Therefore, CCNP solutions in the concentration of 0.01 to 0.05 mg/l do not cause phytotoxicity in the studied plant object A. cepa. Phytotolerance to these concentrations of nanoparticles in A. cepa is high and reaches 80.84% – 92.81%. The obtained indicators of phytotolerance of the studied object A. cepa to CCNP indicate the prospects of their use in the range of concentrations of 0.01 – 0.05 mg/l in the technologies of growing agricultural plants.

Table 2

Morphometric parameters of the roots of *Allium cepa* bulbs grown on solutions of chrome citrate nanoparticles

Name of samples	Concentration of nanoparticles, mg/l	Length of roots, mm M ± m	* IFT%, (phytotoxicity level)	*IT%
K	Control	33,4±3,0	0	100
D1	0.01	31.0±3.2 t=0.55; p=0.58	7.19 (missing)	92.81
D2	0.05	27.0±3.1 t=1.48; p≤0.14	19.16 (missing)	80.84
D3	0.10	24.5±2.4 t=2.33; p=0.02	26.65 (average)	73.35
D4	0.50	18.2±2.1 t=4.15; p≤0.01	45.51 (above average)	54.49
D5	1.00	11.30±1.9 t=6.22; p≤0.01	66.17 (high)	33.83
D6	5.0	0.00	100 (maximum)	0
D7	10.0			

IFT% - phytotoxicity index
IT% - level of tolerance

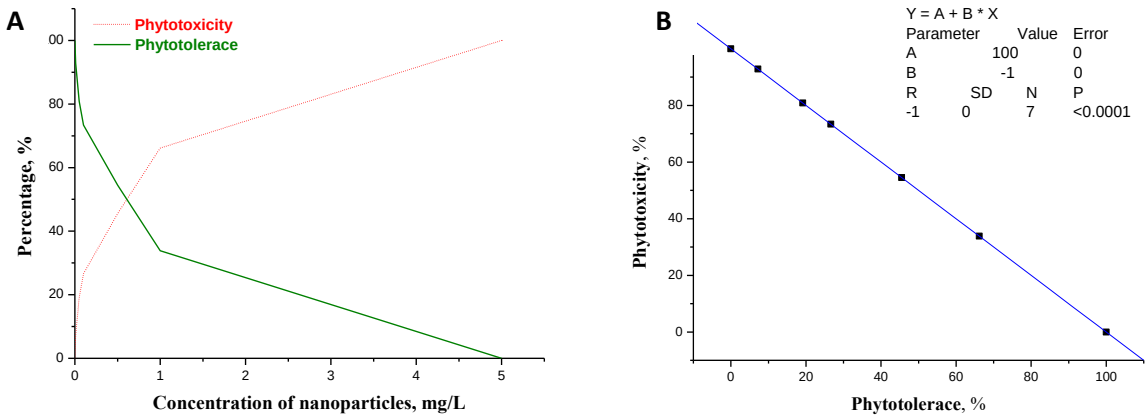

Fig. 2. A. Phytotoxic effect of CCNP on the growth activity of the roots of A. cepa bulbs B. Correlation between phytotoxicity of increasing concentrations (from 0 to 5.0 mg/l) of CCNP and phytotolerance of A. cepa bulb roots to them

Research of cytotoxicity of CCNP by *Allium* test.

One of the indicators assessing the degree of influence of various factors on changes in the structural and functional characteristics of cells is the level of mitotic activity (Fiskesjo, 1997). In this regard, we determined the mitotic activity in the proliferative cells of the apical meristem of *A. cepa* roots. The cytotoxicity of CCNP solutions was assessed in the *Allium* test by the mitotic activity of the meristem cells of the root bulbs of the test object. At the same time, in the *Allium* test we analyzed the mitosis modifying effect of nanoparticle solutions, which meant as a violation of the passage of cells of the meristem of the test object of the phases of mitosis, and the cytotoxic effect – inhibition of cell proliferation.

The mitotic index (MI%) of the apical meristem of the test object was the indicator of mitotic activity, and the cytotoxicity index was the indicator of cytotoxicity for nanoparticle solutions relative to the test object.

For this purpose, cytopreparations were prepared from apical parts (meristems) of *A. cepa* bulb roots grown in CCNP solutions with concentrations that did not cause high phytotoxicity to the test object in the growth test. Because the cytotoxicity of the test substances can be manifested at different stages of the cell cycle, the cell distribution of the primary meristem of *A. cepa* depending on the phase of mitosis was studied (Fiskesjo, 1997). To detect targets of mitosomodifying action of solutions nanoparticles, the phase indices of the cells of the meristems of the test object at different stages of mitosis were determined (see *Figure 3* & *Figure 4*).

As can be seen (*Figure 3*), the mitotic indices of the test object meristems of experimental samples D1 and D2 are close to the control (MI=80.60), and the cytotoxicity indices of the corresponding CCNP solutions are low (1.71 and 3.83, respectively). The phase indices of pro-, meta-, ana- and telophase meristems of the test object in experimental samples D1 and D2 are also close to control and fluctuate within the norm. Thus, the mitotic and phase indices of mitotic activity of *A. cepa* meristem indicate the absence of cytotoxic and mitosis modifying effect of CCNP in the concentration range of 0.01 - 0.05 mg/l relative to the test object.

The mitotic index of the meristem for the test object D3 (see Figure 3) decreases to 62.88, and the index of cytotoxicity, respectively, increases to 21.98. As can be seen from Figure 4, the indices of the phase indices of the meristem of A. cepa of this experimental sample D3 are also different from the control. Mitotic cells have the highest rate in the prophase state (54.13%), indicating a delay in the processes at this stage of mitosis. The prophase index of variant D3 increases by 7% compared to the control (PIK = 47.00%) and significantly exceeds it by 1.15 times. The phase indices of meta-, ana- and telophases, respectively, decrease compared to the control by 2-3%. Lower phase indices indicate a delay in the mitotic activity of the meristems of

the test object at the prophase stage, which may be associated with the negative effect of 0.10 mg/l CCNP solution on the processes of chromosome condensation and redistribution (Konotop, 2019).

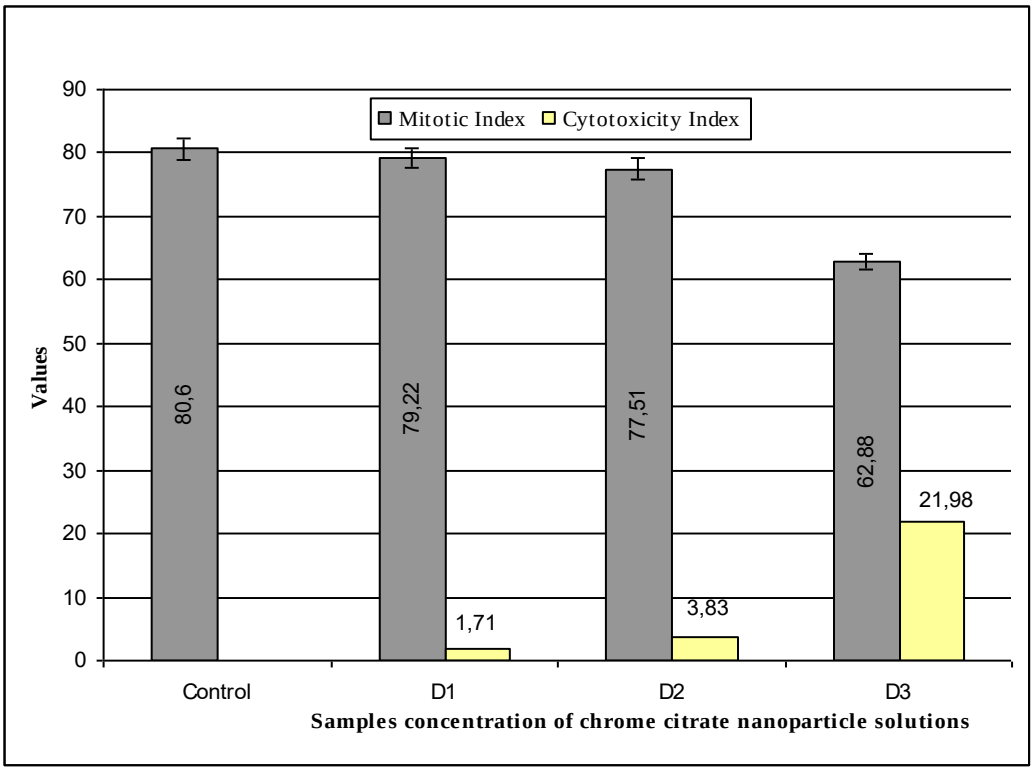

Fig. 3. Mitotic and cytotoxicity indexes of the apical meristem of the roots of Allium cepa bulbs grown on solutions of chrome citrate nanoparticles: D1 – 0.01 mg/l; D2 – 0.05 mg/l; D2 – 0.1 mg/l.

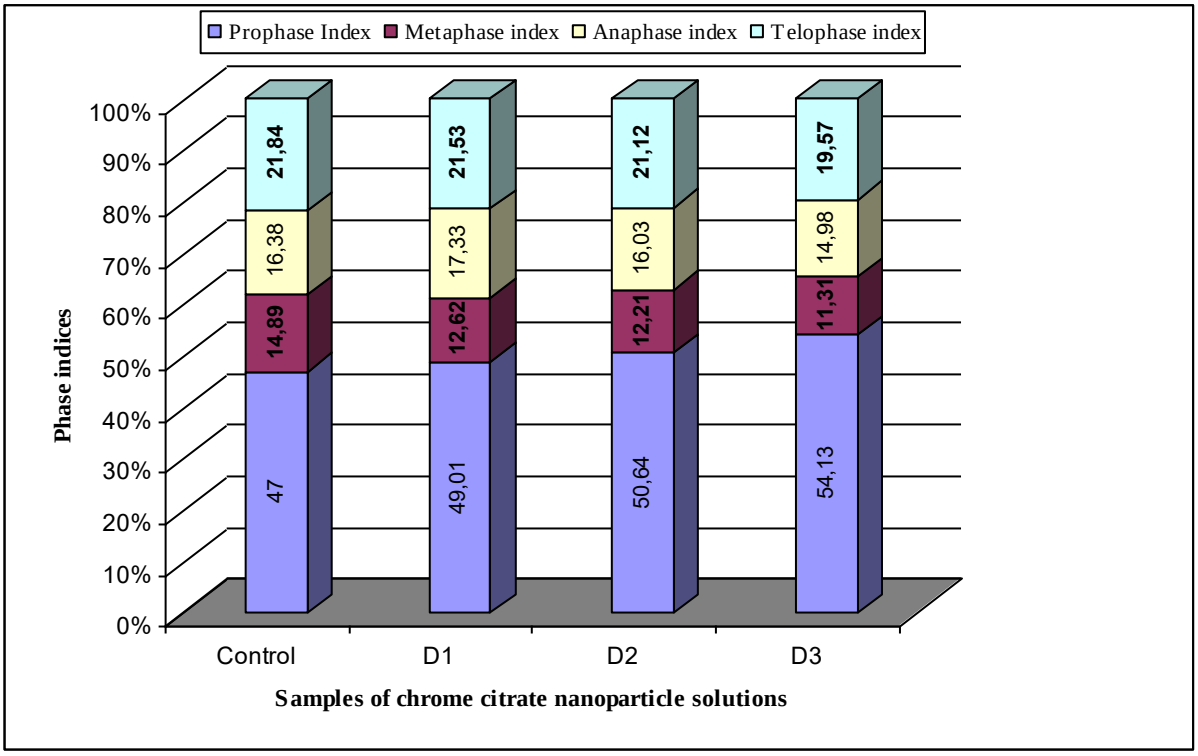

Fig. 4. Mitotic activity of cells in the apical meristem of the roots of Allium cepa bulbs grown on solutions of chrome citrate nanoparticles: D1 – 0.01 mg/l; D2 – 0.05 mg/l; D2 – 0.1 mg/l.

Thus, the results of the studies indicate an average level of cytotoxicity of 0.10 mg/l CCNP solution relative to the test object, which is consistent with our previous data (see above): the level of phytotoxicity of the same solution of nanoparticles close to the growth activity of roots *A. cepa* is average.

Conclusions

Growth *Allium* test revealed that CCNP solutions in the concentration range of 0.01-0.05 mg/l did not cause phytotoxic effects on *A. cepa* at the organism level: they do not cause changes in the turbidity, color, and shape of the tips of their roots, growth activity – the length of the roots of the test samples does not differ significantly from the control. The phytotolerance of the roots of *A. cepa* bulbs to these concentrations of nanoparticles is high and reaches 80.84% – 92.81%.

It was determined that CCNP in the range of concentrations of 0.01-0.05 mg/l in the *Allium* test did not show mito- and cytotoxicity and mitosis modifying effect on the proliferative activity of cells of the test object meristem: mitotic and phase indices are within normal limits; cytotoxicity indices are within the background values.

It was found that CCNP in the concentration range of 0.05-10.00 mg/l caused phytotoxic effects of different levels on the growth activity of the test object roots. In particular, the phytotoxicity of nanoparticles in the concentration range from 0.05 to 0.10 mg/l is of average level; in the field of concentrations from 0.10 to 0.50 mg/l – above average, in the range of concentrations from 0.50 to 1.00 mg/l – high; in the field of concentrations from 5 to 10 mg/l maximum.

It was determined that CCNP at a concentration of 0.1 mg/l showed cytotoxicity and mitosis modifying effect on the test object: the mitotic index of the meristem *A. cepa* decreases, phase indices differ from standard, there is a delay in chromosome spiraling at the level prophase: the level of cytotoxicity of this solution of nanoparticles against *A. cepa* is average.

The obtained research results confirm the possibility of using CCNP in technologies of growing crops in the range of biologically acceptable concentrations (0.01-0.05 mg/l), which do not reveal any manifestations of phyto-, mito- and cytotoxicity.

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CHAPTER 3. ACTUAL PROBLEMS AND EDUCATIONAL ASPEMTS OF THE SPEMIALTY 226 "PHARMACY, INDUSTRIAL PHARMACY"

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Abstract. *Ensuring the monitoring of the quality of educational services and the educational process in higher education institutions (HEIs), that offer Educational Programs to train specialists in medical and pharmaceutical branches is one of the health care obligations that Ukraine as a state undertakes. Traditionally, specialists for pharmaceutical manufacturing were trained mostly at the HEIs, which were subordinated to the Ministry of Education and Science of Ukraine (MES), and those for pharmacies and hospital pharmacies were trained at the HEIs, subordinated to the Ministry of Health of Ukraine (MOH).*

In 2016, a single specialty 226 "Pharmacy" was introduced, and in 2017 the title name of the specialty was specified as 226 "Pharmacy, Industrial Pharmacy". The draft of Resolution of the Cabinet of Ministers of Ukraine (CMU) "On the Amendments to the List of a branch of knowledge and specialties for higher education" provides dividing of the specialty 226 "Pharmacy, Industrial Pharmacy" into two separate specialties: 226 "Pharmacy", which remains in the branch of knowledge 22 "Health Care", and 188 "Industrial Pharmacy", which potentially will be transferred to the branch of knowledge 18 "Manufacturing and Technology". The dividing of specialty into two separate ones is pertinent; however, the problem of transfer significantly affects the training of highly qualified human resources. That is why it is important to take out this problem from a limited circle of specialists in the pharmaceutical branch to the general public.

The research aimed to study and summarize the legislation on the current state of specialists training for the pharmaceutical branch by the specialty 226 "Pharmacy, Industrial Pharmacy", as well as the search for possible ways to solve the educational problem. The following methods were applied: meta-analysis, desk research, comparative analysis and modeling.

It is established the necessity to save the specialty "Industrial Pharmacy" in the field of knowledge 22 "Health Care", as its removal levels the results of specialists training and makes it impossible for the functioning pharmaceutical industry of Ukraine. As a result of this process, obstacles will be created for the research realization, development, and implementation of new medicines and generic drugs. It is extremely important to save the specialty "Industrial Pharmacy" in the field of knowledge 22 "Health Care". This is the only possible way to guarantee the quality of the drugs according to the Complex of Good Pharmaceutical Practices (GMP, GLP, GCP, GDP, GPP, GSP, GEP, GPEP) at all stages of its promotion from manufacturer to the patient, that will facilitate scientific research and development of new safe, effective, high-quality

medicines, and also will allow providing training of highly skilled specialists for pharmaceutical branch.

Keywords: *healthcare, pharmacy, industrial pharmacy, legislative documents, branch of knowledge, specialty.*

Introduction. Maintaining the health of the citizens of their country is one of the main tasks of the state. It should be noted that our state, according to the Constitution of Ukraine and other regulations, undertakes a number of very important obligations regarding health care (Constitution of Ukraine, 2020; Law of Ukraine № 27, 2021; Law of Ukraine № 23, 2019). Among them are not only functions related to organizational, legislative, validation, certification, licensing, controlling processes, but also to ensure monitoring the quality of educational services and the educational process in higher education institutions (HEIs).

It is known, the most of the HEIs are subordinated to the Ministry of Education and Science of Ukraine (MES) and only medical and pharmaceutical HEIs are subordinated to the Ministry of Health of Ukraine (MOH). However, the adoption of a number of legislative acts for the past five years has led to certain problems in the pharmaceutical industry, which begin from the specialist's training and the provision of quality educational services. Traditionally, specialists for pharmaceutical manufacturing were trained mostly at the HEIs, which were subordinated to the MES, and those for pharmacies and hospital pharmacies were trained at the HEIs, subordinated to the MOH. But the situation has changed dramatically since 2015/2016.

Analysis of recent publications. According to the Resolution of the Cabinet of Ministers of Ukraine (CMU) "On approval of the list of the branch of knowledge and specialties for which the training of higher education applicants" on 29.04.2015, specialty "Pharmaceutical Technology" was removed, renamed and referred to another branch of knowledge – 22 "Health Care", specialty 226 "Pharmacy" (Resolution of Cabinet of Ministers № 266, 2015). In 2017, according to the Resolution of the CMU № 53 on 01.02.2017, this specialty was renamed as 226 "Pharmacy, industrial pharmacy" (.Resolution of Cabinet of Ministers № 53, 2017). The problematic issues of pharmaceutical education in Ukraine are well known to both scientists and practitioners in the field. The most comprehensive issue of the quality training of specialists nowadays was set out in the speech of the Rector of the National University of Pharmacy (NUPh), Professor Alla Kotvitska (Kotvitska, A. A., 2021).

However, the understanding of artificially created problems, unfortunately, does not allow to easy and quick their solving, because the decisions, approved by legislation, are related to the interests of various structures, and also have a certain period of validity; they are difficult to change immediately.

The purpose of the research. The research aimed to study and summarize the legislation on the current state of specialists training for the pharmaceutical industry by the specialty 226 "Pharmacy, Industrial Pharmacy", as well as the search for possible ways to solve the educational problem. Study objects included legislative acts on training of specialists by the specialty 226 "Pharmacy, Industrial Pharmacy"; study and analysis of educational programs of the HEIs that offered such training. The following methods were applied: meta-analysis, desk research, comparative analysis and modeling.

Presentation of the main material As a result of the renaming and transferring of the specialty, in which the training of technological engineers for pharmaceutical companies was provided, this direction of specialist's training actually found itself in the field of knowledge 22 "Health Care" in framework specialty 226 "Pharmacy".

However, in 2017, when the name of the specialty 226 "Pharmacy, Industrial Pharmacy" was implemented, a conflict of interest arose. Such a title name of the specialty theoretically foresaw that the graduated specialist will be able to immediately work in both pharmacies and industrial pharmaceutical companies. The problem was that no university could provide such education. In order to train a specialist of this level, it would be necessary at first organize learning

in medical (pharmaceutical) HEIs, subordinated to the MOH, and then, to obtain the qualification of technological engineer, – in HEIs, subordinated to the MES.

Actually, all professionals in the field, scientists, government agencies understand the requirement for dividing the specialty 226 "Pharmacy, Industrial Pharmacy" into two separate specialty "Pharmacy" and "Industrial Pharmacy". However, this is not easy to implement for technical reasons. All digital codes are fully used in field of knowledge 22 "Health Care" (Table 1).

Table 1

The list of fields of knowledge and specialties on which training of high education applicants is carried out

Code and name of the field of knowledge	№	Title name of specialty in Ukraine		According to the International Standard Classification of Education	
		Code	Title name of specialty	Code	Title name of the corresponding detailed branch
22 Health Care	1	221	Dentistry	0911	Dental Studies
	2	222	Medicine	0912	Medicine
	3	223	Nursing	0913	Nursing and Midwifery
	4	224	Medical Diagnostic and Treatment Technology	0914	Medical Diagnostic and Treatment Technology
	5	225	Medical Psychology	0313	Psychology
	6	226	Pharmacy, Industrial Pharmacy	0588	Inter-disciplinary programs and qualifications involving natural sciences, mathematics and statistics
				0711	Chemical Engineering and Processes
				0916	Pharmacy
	7	227	Physical Therapy, Ergotherapy	0915	Therapy and Rehabilitation
	8	228	Pediatry	0912	Medicine
	9	229	Public Health	0413	Management and Administration

On August 13, 2021, the MEH proposed for public discussion a draft of Resolution "On the Amendments to the List of a branch of knowledge and specialties for higher education", provides dividing of the specialty 226 "Pharmacy, Industrial Pharmacy" into two separate specialties: 226 "Pharmacy", which remains in the branch of knowledge 22 "Health Care", and 188 "Industrial Pharmacy", which potentially will be transferred to the branch of knowledge 18 "Manufacturing and Technology".

The division of specialty 226 "Pharmacy, Industrial Pharmacy" into two separate ones, is expedient and timely. However, in our strong belief, the specialty "Industrial Pharmacy" should be saved in the field of knowledge 22 "Health Care". For this reason we propose to enter a separate code 226.1 for specialty "Industrial Pharmacy". At the same time, it should be predicted that the specialist's training in the specialty "Industrial Pharmacy" can be provided in the HEIs, which are subordinated to both the MOH and the MES. The training of the last one should be conducted according to the two-degree system of education (the first – bachelor's degree and the second – master's degree of higher education), and, respectively, the defense of bachelor's / master's qualification project should remain as the form of final certification. It would be expedient legislatively to provide an opportunity for applicants for higher education in the direction "Pharmacy" and "Industrial Pharmacy" to receive a second higher pharmaceutical education across passing the STEP 1 exams in the 4th year of study for direction "Industrial Pharmacy" and across defense the bachelor's qualification project for direction "Pharmacy" and the possibility of parallel training in the appropriate specialization.

Another alternative way may be a proposal to release the code 228 for separated specialty "Industrial Pharmacy" by combining the specialties "Medicine" and "Pediatrics" into a single specialty – "Medicine", as according to the International Standard Classification of Education, code and title name of the relevant detailed field is the same – 0912 Medicine.

It is extremely important to save the specialty "Industrial Pharmacy" in the field of knowledge 22 "Health Care". This is based on a deep understanding of a single logically related legal framework, which is formed for both the pharmaceutical industry and the intermediary level (pharmaceutical companies and pharmacies) in the health care field in Ukraine.

Relevant specialist's training within the given specialty of the second (master's) degree of higher education based on the first (bachelor's) degree is provided at the leading domestic universities, including: Kyiv National University of Technologies and Design (Kyiv), Lviv Polytechnic National University (Lviv), Institute of Chemicals Technologies of the Volodymyr Dahl East Ukrainian National University (Dnipro), Ukrainian State University of Chemical Technology (Kyiv), Odessa Polytechnic State University (Odessa), which are subordinated to the MES, as well as the NUPh (Kharkiv), which is subordinated to the MOH.

According to the resolution of the CMU № 497 on 19.05.2021, specialty 226 "Pharmacy, Industrial Pharmacy" of the branch of knowledge 22 "Health Care" included in the List of specialties for which an single state qualifying examination (SSQE) is a form of final certification of master's degree applicants (Resolution of Cabinet of Ministers № 497, 2021). According to the resolution of the CMU № 334 on 28.03.2018, the MOH conducts an SSQE in the STEP 2 format for master's degree applicants, who are training based on the complete general secondary education (Resolution of Cabinet of Ministers, 2018).

The training specialists of the second (masters) degree of higher education in the field of "Industrial Pharmacy" is provided based on the bachelor's degree program, which does not require passing the STEP 1 exam. Nowadays, for such a master's degree program the SSQE STEP 1 and SSQE STEP 2 have not been developed. At the same time, it is determined that the defense of the master's qualification project is the only a form of certification of master's degree applicants. The aim of the program is to acquire the general and special competencies for professional activities in the relevant position in the field of industrial production of medicines. From 2022 the SSQE becomes a mandatory component of the individual curriculum of the student, and the curricula for the 2021-2022 academic years at the Lviv Polytechnic National University have already been approved, that's why making appropriate changes is impossible. It is, therefore, necessary to provide for an intermediate period for the implementation of the STEP 1 and STEP 2 exam systems.

For making comparative analysis, we considered the list of disciplines approved by the Educational and Professional Program (EPP) of Danylo Halytsky Lviv National Medical University, for the training of specialists of the second (master's) degree of higher education of the specialty 226 "Pharmacy, Industrial Pharmacy", and a list of educational components for the applicants of first (bachelor's) and for the second (master's) degree of higher education of the specialty 226 "Pharmacy, Industrial Pharmacy", trained at the Lviv Polytechnic National University (Table 2, 3, 4, 5).

Table 2

The list of educational components of EPP "Pharmacy, Industrial Pharmacy" in Danylo Halytsky Lviv National Medical University

Subject matter code	Curriculum unit (subject matter, course projects, practical training, qualification project)	Number of credits	Form of final control
1	2	3	4
Obligatory EPP component			
Humanitarian training			
ОС 1.	The Ukrainian Language (professional-oriented)	3	Credit
ОС 2.	History of Ukraine and Ukrainian Culture	3	Credit

OC 3.0.	Philosophy	3	Credit with the mark
OC 3.1.	Bioethics	0,5	Credit
OC 4.	The Foreign Language (professional-oriented)	5	Examination
	Total	***14,5***	
	Fundamental training		
OC 5.	Latin	3	Credit
OC 6.	Human Anatomy	3	Credit
OC 7.	Physiology	4	Examination
OC 8.	Biological physics and physical methods of analysis	4,5	Examination
OC 9.	Biology with essential genetics	3	Examination
OC 10.	Higher mathematics and statistics	4	Examination
OC 11.	General and inorganic chemistry	9	Examination
OC 12.	Information technologies in pharmacy	4	Credit with the mark
OC 13.	Analytical chemistry	8	Examination
OC 14.	Organic chemistry	8	Examination
OC 15.	Pharmaceutical botany	5	Examination
OC 16.	Microbiology and essential immunology	5	Examination
OC 17.	Physical and Colloid chemistry	5	Examination
OC 18.	Biological chemistry	6	Examination
OC 19.	Ethics an deontology in pharmacy	2	Credit
OC 20.	Pathological physiology	5	Examination
OC 21.	Computer simulation in pharmacy	3	Credit
OC 22.	Medicine of extreme conditions	2	Credit
	Total	***83,5***	
	Vocational training		
OC 23.	Hygiene in pharmacy and ecology	3	Credit
OC 24.	Pharmacology	9	Examination
OC 25.	Pharmacognosy	9	Examination
OC 26.	Law and legislation in Pharmacy	2	Credit
OC 27.	Pharmaceutical chemistry	14	Examination
OC 28.	Pharmacotherapy with pharmacokinetics	3	Examination
OC 29.	Health care management	3	Credit
OC 30.	Technology of medicines	13	Examination
OC 31.	Organization and economics in pharmacy	7	Examination
OC 32.	The study of pharmaceutical and medical commodities	4	Examination
OC 33.	Management and marketing in pharmacy	9	Examination
OC 34.	Clinical pharmacy and pharmaceutical care	9	Examination
OC 35.	Toxicological and forensic chemistry	6	Examination
OC 36.	Biopharmacy	3	Credit
OC 37.	Appropriate practices in pharmacy	3	Credit
OC 38.	The resource study of medicinal plants	3	Credit
OC 39.	Standardization of medicines	3	Credit
OC 40.	Technology of cosmetics	3	Credit
OC 41.	Pharmaceutical biotechnology	3	Credit
OC 42.	Quality assessment system in pharmacy	3	Credit
OC 43.	Social pharmacy	3	Credit
OC 44.	Military oriented pharmacy training	3	Credit
	Total	*118*	
	Industrial practice		
OC 45.	Introductory practice on the organization and economics in pharmacy	1,5	Credit with the mark
OC 46.	Propaedeutic practice on pharmacy medicines technology	1,5	Credit with the mark

OC 47.	First preliminary aid with the introductory medical practice	3	Credit
OC 48.	Field practice in pharmaceutical botany	3	Credit with the mark
	Total	*9*	
	Total for the vocational training	***127***	
General amount of the obligatory program units		**225**	
Elective components of the Curriculum*			
Elective module 1			
EM 1.1.	The Foreign Language (second)	9	Credit
EM 1.2.	The English Language	12	Credit
EM 1.3.	Modern problems of molecular biology	3	Credit
EM 1.4.	Modern problems of biophysics	3	Credit
EM 1.5.	Physical and chemical methods of analysis	3	Credit
EM 1.6.	Biological role of vital elements	3	Credit
EM 1.7.	Theory of knowledge and pharmacy	3	Credit
EM 1.8.	Sociology and medical sociology	3	Credit
EM 1.9.	Psychology of communication	3	Credit
EM 1.10.	Theory and practice of professional communication	3	Credit
EM 1.11.	History of medicine and pharmacy	3	Credit
EM 1.12	Security of vital activity and biological security	3	Credit
EM 1.13.	Political science	3	Credit
EM 1.14.	Fundamentals of Cristian ethics and moral	3	Credit
EM 1.15.	Basics of computer technologies in pharmacy	3	Credit
EM 1.16.	Pharmaceutical informatics and statistics	3	Credit
EM 1.17.	Principles of systemic analysis	3	Credit
EM 1.18.	Basics of chemical metrology	3	Credit
EM 1.19.	Identification of organic compounds	3	Credit
EM 1.20.	Modern analytical laboratory practice	3	Credit
EM 1.21.	Principles of social psychology	3	Credit
EM 1.22.	Medicinal plants of pharmacy	3	Credit
EM 1.23.	First aid in the pharmaceutical institutions	3	Credit
EM 1.24.	Pathological physiology of civilization diseases	3	Credit
EM 1.25.	Chemistry of medicines	3	Credit
EM 1.26.	Modern methods of investigating biological systems	3	Credit
EM 1.27.	Metabolism of drugs	3	Credit
EM 1.28.	World pharmaceutical industry	3	Credit
EM 1.29.	Mechanism of pharmacological activity and toxicity of drugs	3	Credit
EM 1.30.	Pharmaceutical aspects of toxicomania	3	Credit
EM 1.31.	Pharmaceutical aspects of phytotherapy	3	Credit
EM 1.32.	Microorganism in biotechnological processes	3	Credit
EM 1.33.	Basics of economics in pharmacy	3	Credit
EM 1.34.	Ethical problems in pharmacy	3	Credit
EM 1.35.	Limited batch production of medicine	3	Credit
EM 1.36.	Drugs development	3	Credit
EM 1.37.	Theoretical principles of synthesis and the relation between the structure and the effect of medicines	3	Credit
EM 1.38.	Quality control of medicines	3	Credit
EM 1.39	Investigation of the pharmaceutical market	3	Credit
EM 1.40.	Side effects of drugs	3	Credit
EM 1.41.	Pharmacogenetics	3	Credit
EM 1.42.	Pharomacology	3	Credit
EM 1.43.	Basics of clinical medicine	3	Credit
EM 1.44.	Basics of medical standardization and evidence	3	Credit

	medicine		
EM 1.45.	Drug-related problems	3	Credit
EM 1.46.	Modern medical products	3	Credit
EM 1.47.	Logistic in pharmacy	3	Credit
EM 1.48.	Pharmaceutical aspects of nutriciology (biological active additives)	3	Credit
EM 1.49.	Ecotoxicology	3	Credit
EM 1.50.	Chemical and toxicological analysis	3	Credit
EM 1.51.	Medicinal plants and phytotherapy	3	Credit
EM 1.52.	Physical training	6	Credit
EM 1.53.	Patentology	3	Credit
Elective module 2			
EM 2.1.	Industrial practice in pharmacognosy	3	Credit with the mark
EM 2.2	Industrial practice in the technology of drugs	6	Credit with the mark
EM 2.3.	Industrial practice in organization and economics in pharmacy	5	Credit with the mark
EM 2.4.	Industrial practice in management and marketing in pharmacy	4	Credit with the mark
EM 2.5.	Industrial practice in pharmaceutical chemistry	5	Credit with the mark
EM 2.6	Industrial practice in clinical pharmacy	1	Credit with the mark
EM 2.7.	Industrial practice in clinical pharmacy and pharmaceutical care	5	Credit with the mark
EM 2.8.	Industrial practice in pharmacoeconomics	1	Credit with the mark
EM 2.9.	Industrial practice in pharmaceutical information	4	Credit with the mark
Elective module 3			
EM 3.1.	Methodology of scientific investigations on the technology of drugs based on the subject of Master's degree paper	15	Defense of a Master's Degree Paper
EM 3.2.	Methodology of scientific investigations on pharmaceutical chemistry based on the subject of Master's degree paper	15	Defense of a Master's Degree Paper
EM 3.3.	Methodology of scientific investigations on the pharmacognosy based on the subject of Master's degree paper	15	Defense of a Master's Degree Paper
EM 3.4.	Methodology of scientific investigations on organization and economics in pharmacy based on the subject of Master's degree paper	15	Defense of a Master's Degree Paper
EM 3.5.	Methodology of scientific investigations on the clinical pharmacy based on the subject of Master's degree paper	15	Defense of a Master's Degree Paper
EM 3.6.	Methodology of scientific investigations on the toxicological and forensic chemistry based on the subject of Master's degree paper	15	Defense of a Master's Degree Paper
General amount of the elective program units		**75**	
GENERAL AMOUNT OF THE SYTLLABUS		**300**	

Table 3

The list of educational components of EPP "Pharmacy, Industrial Pharmacy" for the first (bachelor's) degree of higher education in Lviv Polytechnic National University

Subject matter code	Curriculum unit (subject matter, course projects, practical training, qualification project)	Number of credits	Form of final control
1	2	3	4
Common components of educational and professional programs			
1. The cycle of general training			
OC 1.1.	Higher mathematics, part 1	6	Examination
OC 1.2.	The Foreign Language (professional-oriented), part 1	3	Credit with the mark
OC 1.3.	History of statehood and culture of Ukraine	3	Examination
OC 1.4.	Chemistry 1 (general and inorganic chemistry)	5	Examination
OC 1.5.	Chemistry 2 (organic chemistry), part 1	9	Examination
OC 1.6.	Higher mathematics, part 2	6	Examination
OC 1.7.	The Foreign Language (professional-oriented), part 2	3	Credit with the mark
OC 1.8.	The Ukrainian Language (professional-oriented)	3	Examination
OC 1.9.	Physics	7	Examination
OC 1.10.	Physical and Colloid chemistry	7	Examination
OC 1.11.	Chemical methods of analysis of substances	4	Credit with the mark
OC 1.12.	Biology and physiology with basic of anatomy	7	Examination
OC 1.13.	The Foreign Language (professional-oriented), part 3	3	Examination
OC 1.14.	Microbiology	7	Examination
OC 1.15.	Physical and chemical methods of analysis of substances	4	Credit with the mark
OC 1.16.	Biological chemistry and molecular biology	8	Examination
OC 1.17.	Informatics	3	Credit with the mark
OC 1.18.	Philosophy	3	Examination
Total for the cycle		***91***	
2. The cycle of professional training			
OC 2.1.	Introduction to the profession and the basics of professional hygiene	4	Credit with the mark
OC 2.2.	Latin	3	Credit with the mark
OC 2.3.	Methods of organic synthesis	6	Examination
OC 2.4.	Medical botany	6	Examination
OC 2.5.	Toxicological chemistry	4	Examination
OC 2.6.	Drugs technology in pharmacy	6	Examination
OC 2.7.	Engineering and computer graphics	4	Credit with the mark
OC 2.8.	Processes and devices of pharmaceutical manufacturing	5	Examination
OC 2.9.	Fundamentals of labor protection and life safety	3	Examination
OC 2.10.	Pharmacognosy	5	Examination
OC 2.11.	Pharmaceutical chemistry	7	Examination
OC 2.12.	Organization and economics in pharmacy	3	Examination
OC 2.13.	Basic of pharmacology	4	Examination
OC 2.14.	Drugs technology in pharmacy, Course Project	2	Credit with the mark
OC 2.15.	Pharmacognosy, Course Project	2	Credit with the mark

OC 2.16.	Organization and economics in pharmacy, Course Project	2	Credit with the mark
OC 2.17.	Processes and devices of pharmaceutical manufacturing, Course Project	3	Credit with the mark
OC 2.18.	Educational practice in botany	3	Credit with the mark
OC 2.19.	Drugs technology in pharmacy (industrial practice)	1,5	Credit with the mark
OC 2.20.	Technological practice (industrial practice)	1,5	Credit with the mark
OC 2.21.	Practice on the topic of the bachelor's degree qualification project	4,5	Credit with the mark
OC 2.22.	Performing of the bachelor's degree qualification project	9	Credit with the mark
OC 2.23.	Defense of the bachelor's degree qualification project		
Total for the cycle		***88,5***	
General amount of the obligatory program units		**179,5**	
Elective components of the Curriculum			
1. The cycle of general training			
Total for the cycle		***6***	
2. The cycle of professional training			
Elective components of EPP. Cycle 0100 «Industrial Pharmacy»			
EM 1.1.	Regulatory support of pharmaceutical industries	3	Examination
EM 1.2.	Basic of laboratory and functional diagnostics	3	Credit with the mark
EM 1.3.	Pharmacokinetics	3	Credit with the mark
EM 1.4.	Chemical and technology of medical compounds	7	Examination
EM 1.5.	Basic of clinical pharmacy	4	Credit with the mark
EM 1.6.	Basic of pharmacotherapy	4	Credit with the mark
EM 1.7.	Technology of drugs from natural raw materials and phytotherapy	5	Examination
EM 1.8.	Equipment and design of pharmaceutical industries	5	Examination
EM 1.9.	Management, marketing and pharmaceutical commodity science	4	Examination
EM 1.10.	Basics of emergency medical care	3,5	Credit with the mark
EM 1.11.	Physical methods of drugs' analysis	4	Examination
EM 1.12.	Equipment and design of pharmaceutical industries, Course Project	3	Credit with the mark
Total for the cycle		***48,5***	
Cycle 0200 «Pharmacy»			
EM 2.1.	Laboratory and functional diagnostics and clinical pharmacy	6	Credit with the mark
EM 2.2.	Regulation and legislation of pharmaceutical companies	3	Examination
EM 2.3.	Technology of antibiotics and vitamins	3	Examination
EM 2.4.	Chemistry and technology of drugs	4	Examination
EM 2.5.	Design of chemical and pharmaceutical manufactures	5	Examination
EM 2.6.	Technology of galenical preparations	4	Examination
EM 2.7.	Pharmacology	6	Examination
EM 2.8.	Chemistry of cancerogens	3	Credit with the mark
EM 2.9.	Medical and pharmaceutical commodity science	4	Credit with the

			mark
EM 2.10.	Management and marketing in pharmacy	4	Credit with the mark
EM 2.11.	First aid	3,5	Credit with the mark
EM 2.12.	Design of chemical and pharmaceutical manufactures, Course Project	3	Credit with the mark
Total for the cycle		***48,5***	
General amount of the elective program units		**75**	
Elective components of others EPP			
Total		***6***	
General amount of the elective program units		**60,5**	
GENERAL AMOUNT OF THE SYTLLABUS		**240**	

Table 4

The list of educational components of EPP "Pharmacy, Industrial Pharmacy" for the second (master's) degree of higher education in Lviv Polytechnic National University

Subject matter code	Curriculum unit (subject matter, course projects, practical training, qualification project)	Number of credits	Form of final control
1	2	3	4
Obligatory EPP component for specialty			
1. The cycle of general training			
OC 1.1.	Economics of chemical and pharmaceutical enterprises	4	Examination
Total for the cycle		***4***	
2. The cycle of professional training			
OC 2.1.	Modeling and design of chemical and pharmaceutical enterprises in the GMP system	6	Examination
OC 2.2.	Scientific aspects of ecology of chemical and pharmaceutical industries	4	Credit with the mark
OC 2.3.	Scientific aspects of technology of veterinary and biomedical drugs	7	Credit with the mark
OC 2.4.	Industrial technology of pharmaceutical manufacturing, part 1	6	Examination
OC 2.5.	Occupational and civil safety	3	Credit with the mark
OC 2.6.	Industrial equipment of chemical and pharmaceutical enterprises	3	Examination
OC 2.7.	Modeling and design of chemical and pharmaceutical enterprises in the GMP system, Course Project	3	Credit with the mark
OC 2.8.	Practice on the topic of the master's degree qualification project	9	Credit with the mark
OC 2.9.	Performing of the master's degree qualification project	16,5	
OC 2.10.	Defense of the master's degree qualification project	4,5	
Total for the cycle		***62***	
General amount of the obligatory program units		**66**	
Elective components of the Curriculum			
1. *The cycle of general training*			
Disciplines of the student's choice			
Total for the cycle		***3***	Credit with the mark
2. *The cycle of professional training*			
Elective components of cycle 01 «Industrial Pharmacy»			

EM 1.1.	Quality control of medicines	3	Credit with the mark
EM 1.2.	Industrial technology of pharmaceutical manufacturing, part 2	4	Examination
EM 1.3.	Technology of biologically active substances, biomedical polymers and nanostructures	5	Credit with the mark
EM 1.4.	Technology and application of medical cosmetics	4	Credit with the mark
Total for the cycle		***16***	
Elective components of cycle 02 «Pharmacy»			
EM 2.1.	Clinical Pharmacy	4	Credit with the mark
EM 2.2.	Scientific aspects of biopharmacy	4	Credit with the mark
EM 2.3.	Quality assessment of medicines	4	Examination
EM 2.4.	Pharmacotherapy	4	Credit with the mark
Total for the cycle		***16***	
Disciplines of the student's choice			
Total for the cycle		***5***	Credit with the mark
General amount of the elective program units		**24**	
GENERAL AMOUNT OF THE SYTLLABUS		**90**	

Table 5

The list of educational components of educational scientific program (ESP)
"Pharmacy, Industrial Pharmacy"
for the second (master's) degree of higher education in Lviv Polytechnic National University

Subject matter code	Curriculum unit (subject matter, course projects, practical training, qualification project)	Number of credits	Form of final control
1	2	3	4
Obligatory ESP component for specialty			
	1. The cycle of general training		
OC 1.1.	Economics of chemical and pharmaceutical enterprises	4	Examination
Total for the cycle		***4***	
	2. The cycle of professional training		
OC2.1.	Modeling and design of chemical and pharmaceutical enterprises in the GMP system	6	Examination
OC 2.2.	Scientific aspects of ecology of chemical and pharmaceutical industries	4	Credit with the mark
OC 2.3.	Scientific aspects of technology of veterinary and biomedical drugs	7	Credit with the mark
OC 2.4.	Industrial technology of pharmaceutical manufacturing, part 1	6	Examination
OC 2.5.	Occupational and civil safety	3	Credit with the mark
OC 2.6.	Industrial equipment of chemical and pharmaceutical enterprises	3	Examination
OC 2.7.	Clinical and pharmaceutical aspects of drugs use (special course, part 3)	3	Examination
OC 2.8	Research and seminars on the subject	9	Credit with the mark
OC 2.9	Fundamentals of fine organic synthesis (special course, part 2)	3	Examination

OC 2.10	Basic of pharmaceutical biochemistry (special course, part 1)	3	Examination
OC 2.11	Workshop on preparing of scientific publications, conference materials and presentations of scientific reports	4,5	Credit with the mark
OC 2.12	Modeling and design of chemical and pharmaceutical enterprises in the GMP system, Course Project	3	Credit with the mark
OC 2.13	Educational and research practice	6	Credit with the mark
OC 2.14	Practice on the topic of the master's degree qualification project	12	Credit with the mark
OC 2.15	Performing of the master's degree qualification project	18	
OC2.16	Defense of the master's degree qualification project	1,5	
Total for the cycle		**92**	
General amount of the obligatory program units		**96**	
Elective components of the Curriculum			
1. The cycle of general training			
Disciplines of the student's choice			
Total for the cycle		***3***	Credit with the mark
2. The cycle of professional training			
Elective components of cycle 01 «Industrial Pharmacy»			
EM 1.1.	Quality control of medicines	3	Credit with the mark
EM 1.2.	Industrial technology of pharmaceutical manufacturing, part 2	4	Credit with the mark
EM 1.3.	Technology of biologically active substances, biomedical polymers and nanostructures	5	Credit with the mark
EM 1.4.	Technology and application of medical cosmetics	4	Credit with the mark
Total for the cycle		**16**	
Elective components of cycle 02 «Pharmacy»			
EM 2.1.	Clinical Pharmacy	4	Credit with the mark
EM 2.2.	Scientific aspects of biopharmacy	4	Credit with the mark
EM 2.3.	Quality assessment of medicines	4	Examination
EM 2.4.	Pharmacotherapy	4	Credit with the mark
Total for the cycle		***16***	
Disciplines of the student's choice			
Total for the cycle		***5***	Credit with the mark
General amount of the elective program units		**24**	
GENERAL AMOUNT OF THE SYTLLABUS		**120**	

Analysis of educational programs of specialty 226 "Pharmacy, industrial pharmacy", which are approved in Lviv Polytechnic National University and Danylo Halytsky Lviv National Medical University for specialists training testifies to a significant amount of common educational components, especially the pharmaceutical direction, that is considered as a positive sign for the creation of future Education Standards. However, it should be noted, that the OPP for the first (bachelor's) degree of higher education in Lviv Polytechnic National University includes a large number of disciplines of the cycle of general and professional training such as Higher Mathematics, Physics, Engineering and Computer Graphics, Processes and devices of pharmaceutical manufacturing, etc., are necessary and considered as fundamentals for further components of the educational program that directly form a specialist in the industrial drugs technology and the acquired competencies allow applicants to successfully perform and defense the bachelor's degree qualification project. The development and approved of the Education Standard in the specialty 226 "Pharmacy, Industrial Pharmacy" is extremely important, because will contribute to a single format and content of the list of components of educational programs, unify the form of final certification, and will guarantee competitiveness in the labor market for all

applicants of higher education. To find a compromise to solve this problem, we have started cooperation with five HEIs, which actually train specialists in the specialty "Industrial Pharmacy", to develop and create a database of questions for the STEP 2 test exam.

At the first stage of our joint research, the lists of disciplines in different HEIs were collected and analyzed, and the structure of the integrated test exam of SSQE STEP 2 for direction "Industrial Pharmacy" was formed (Table 6).

Table 6

Courses for professional training of specialists of the second (master's) degree of higher education in the specialty 226 "Pharmacy, industrial pharmacy" for direction "Industrial Pharmacy"

Lviv Polytechnic National University	Ukrainian State University of Chemical Technology	Odesa Polytechnic State University	Kyiv National University of Technologies and Design	The structure of the integrated test exam SSQE KROC 2, axis 2
Modeling and design of chemical and pharmaceutical enterprises in the GMP system	Automated process control systems	Biotechnology in pharmacy and cosmetology	Industrial biotechnology of drugs	Industrial biotechnology of drugs
Scientific aspects of ecology of chemical and pharmaceutical industries	Validation process	Standardization of drugs	Validation of technological process and analytical methods	Validation process
Scientific aspects of technology of veterinary and biomedical drugs	Modern pharmaceutical technologies	Drugs technology in pharmacy	Technologies of active pharmaceutical ingredients	Modern pharmaceutical technologies
Industrial technology of pharmaceutical manufacturing	Special equipment and design of chemical and pharmaceutical industries	Cosmetic chemistry	Special equipment and design of chemical and pharmaceutical industries	Special equipment and design of chemical and pharmaceutical industries
Industrial equipment of chemical and pharmaceutical enterprises	Pharmaceutical development of drugs	Basic of scientific research in the chemical and pharmaceutical branch	Pharmaceutical development of drugs	Pharmaceutical development of drugs
Quality control of medicines		Automated systems and information technology in pharmacy	Pharmaceutical quality system and quality control of medicines	Pharmaceutical quality system and quality control of medicines
Technology of biologically active substances, biomedical polymers and nanostructures				

Further research will concern the development of a database of questions for the SSQE STEP 1 and STEP 2 exams It would be much easier to create such a database if the Education Standard will be approved and available. However, the elaboration of such a Standard must be

preceded by the division of specialty 226 "Pharmacy, Industrial Pharmacy" into two separate ones - "Pharmacy" and "Industrial Pharmacy", which must belong to the same field of knowledge 22 "Health care".

Conclusions

1. Ukraine as a state, according to the Constitution and other regulations, undertakes a number of very important obligations regarding health care, especially, ensure monitoring the quality of educational services and the educational process in higher education institutions.

2. The specialty "Industrial Pharmacy" should be saved in the field of knowledge 22 "Health Care", as its transfer to the branch of knowledge 18 "Manufacturing and Technology" levels the results of specialists training, threatens the existence of the specialty and makes it impossible for the functioning pharmaceutical industry of Ukraine.

3. As a result of the transfer of specialty "Industrial Pharmacy" from the field of knowledge 22 "Health Care" to the branch of knowledge 18 "Manufacturing and Technology", obstacles will be created for the research realization, development, and implementation of new medicines and generic drugs.

4. It is extremely important to save the specialty "Industrial Pharmacy" in the field of knowledge 22 "Health Care". This is the only possible way to guarantee the quality of the drugs according to the Complex of Good Pharmaceutical Practices (GMP, GLP, GCP, GDP, GPP, GSP, GEP, GPEP) at all stages of its promotion from manufacturer to the patient, that will facilitate scientific research and development of new safe, effective, high-quality medicines, and also will allow providing training of highly skilled specialists for pharmaceutical branch.

5. Traditionally, specialists for pharmaceutical manufacturing were trained mostly at the higher education institutions, which were subordinated to the Ministry of Education and Science of Ukraine, and those for pharmacies and hospital pharmacies were trained at the higher education institutions, subordinated to the Ministry of Health of Ukraine. However, with the introduction in 2016 of a single specialty 226 "Pharmacy", and in 2017 with the renaming of the specialty to 226 "Pharmacy, Industrial Pharmacy", in the higher education institutions of different subordination (Ministry of Health of Ukraine and Ministry of Education and Science of Ukraine) is training professionals for the pharmaceutical industry. The only significant difference is the quality control of student training. In the higher education institutions, subordinated to the Ministry of Health of Ukraine, the assessment system STEP 1, 2, 3 exams has been introduced. In the higher education institutions subordinated to the Ministry of Education and Science of Ukraine, students perform and defense bachelors or master's qualification projects as a form of certification of applicants of the degree of higher education. We completely agree with the requirement to move to a system for assessing the quality of knowledge in accordance with the STEP 1 and STEP 2 exam systems and it is important to ensure a smooth, adequate transition to this system and coordinate the actions of higher education institutions, which found themselves in a similar situation.

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CHAPTER 4. CHANGES IN THE ELECTROPHYSICAL PROPERTIES OF NATURAL DRINKING WATER IN ITS EXPERIMENTAL COHERENCE WITH DIFFERENT POLARITY AND DEGREE

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Abstract. *The article presents experimental studies results on electrophysical properties changes of natural drinking water after its coherence according to the results of Kirlian photography. The study issue is relevant to connection between health water properties and its coherence. The coherent state determines nonlinear effects occurrence, which leads to the water molecules total response to Kirlian irradiation. Gas–discharge glow of 50 drops of each water sample was received on an X–ray film. Water coherence was carried out by using a quantum teleportation system. A coherent state of water was created with different spin directions (right and left) and the degree of coherence (1–3). Computer processing of the Kirlian water droplets photographs was carried out by building brightness histograms. The results were compared with the previously developed by us criteria for median values and the medians difference of the parameters of 12 histogram subranges for experimental standard water samples – distilled, tap water, from natural drinking sources outside and from the territories of monasteries. The indicators differences degree was analyzed according to the Euclidean distances for medians values and differences in medians with each typical water sample. Distilled water was used as an incoherent standard. Various changes patterns of the studied values were obtained for the left and right water polarization of the samples and with an increase in its degree. A step–by–step change in the electrophysical properties of the control samples was observed for both types of their coherence with a smaller interval for the left direction. Levorotatory coherent water acquired new stable properties already during the first impact degree. The established experimental Kirlian characteristics can be used as a water coherence express–test.*

Keywords: *coherent water, Kirlian photography, X–ray film*

Introduction

Until recently, the role of electronically excited states was not taken into account. Nevertheless, the dependence on these states of the biological water properties is known. On the basis of quantum electrodynamics, it was proved that liquid water is a coalition, a set of coherent domains. If the domain is in the lowest energy state (the main state), all electrons are firmly connected. So for water ionization it is required that it receives an energy pulse that corresponds to a soft x–ray radiation. Therefore, in the excited state, many electrons are almost free, and low energy is needed for the electrons to become completely free. In the incoherent state, the water molecule cannot act as electron donor recover, and coherent water is a good reducing agent.

We earlier reported on the use of Kirlianphotography, as a method based on the effect of gas–discharge Kirlian glow around the water droplets, to assess its health properties. Today, some ideas are being developed about connections of the latter with the coherent water state.

Informative signs of images of gas–discharge radiation of water droplets from different natural sources on an X–ray filmwere analyzed, previously scanned. The samples of Kirlian (KI) were formed out of more than 900 drops of typical water samples (TW): distilled – TW 1, plumbing – TW 2, from natural sources – TW 3 and from the territories of monasteries – TW 4).

Since the method of classical Kirlian photography is easy to perform with high informativeness and high sensitivity to external influences, it is advisable to study possibilities of its use in express assessment of water samples coherence condition according to theuse results of Kirlian photography method.

The purpose of the research was to study the changes in the electrophysical properties of experimental coherent natural drinking water at different degrees of opposite polarization in comparison with its control samples.

Material and research methods. Natural drinking water (CDW) was used as a control sample. Its coherenization was performed by using the developed quantum teleportation system described in, with the help of which at a distance of about 500 km (from Kiev to the city of Dnipro) a coherent state of DW with different spin orientation (right and left) and degree of coherencewas created. (1, 2, 3).

A special chip represented the element of a singlent pair with a translation symmetry in the form of a metal plate, 5x5 mm, which was attached to the outside of a glass cup, which was filledwith packed, natural drinking water. The water volume for research was taken in the amount of 50 ml. At the beginning, a L–chip (left–sided orientation of spins) was taken to activate the water, and then the R–chip, which was attached to another cup with the same packaged water. After filling the initial DW into the cups, using measurements of water physical properties, it was observed in the dynamics of "guidance" using chips of the water coherent state.

This method lies in the fact that the introduction of water into the coherent state occurs through spin saturation of water, which is carried out before the process of Kirlian irradiation. Spin saturation is achieved by contacting water with a chip inducer placed on water tanks, and the exposure to water occurs continuously to the irradiation process. As a result of the spin saturation and interaction of the spin–grid (spin–molecule), the water molecular structure begins to oscillatrate with one frequency and with one phase, which leads to the coherent state.

The coherent state determines nonlinear effects appearance, which leads to the total response of water molecules on Kirlian irradiation.

Kirlian photographing was carried out with 50 drops of control and experimental water samples. An X–ray film was used, an experimental device with a console for liquid–phase objects was developed with participation of the "National University of Ukraine's Health Protection. L. Schupika" (Kiev) and NTU "Dniprovskaya Polytechnica" (Dnipro, Ukraine).

To study water properties histograms of image brightness were built, which allow to identify geometric and bright–light (photometric) image parameters. Specific radiation features are highlighted for a specific water type by analyzation and parametrization of brightness histograms. Averaging specific radiation signs for samples within one water type based on calculations of medians and their differences. From the point of view of mathematical statistics it

allowed us to implement a steady (robust) approach to the processing of experimental data, since the median is an experimental assessment of the mathematical expectation, which ensures resistance torandom emission and misses.

As the most likely value of the column height, the magnitude of the median was used, calculated for the corresponding sample of images. The further classification procedure was based on the use of metric – the Euclidean distance between the heights of the corresponding histogram columns. As an additional criterion, the difference of histogram column elements in adjacent intervals were used to compare water samples. They were calculated by subtracting the magnitudes from the subsequent height – the height of the previous interval. The physical meaning of the application of this indicator consists in the possibility of tracking dynamic changes in the brightness indicators from one interval to another histogram interval.

Maximum amplitude in the histogram of brightness corresponds to the background of the X–ray film. For distilled water, without impurities, this peak turns out to be the only extremum for the graph of the image brightness histogram. It is the worst version from the point of view of its quantum and biological properties and can be used as a standard of non–coherent fluid. Its molecular structure is constructed in such a way that it cannot act as a source of free charge carriers. Itis manifested in a weak streamer crown of the luminescence around the drop and the smallest luminescence intensity, compared with other types of water.

For water with impuritiesinclusions, the histogram is multimodal. For a sample of tap water, a substantially pronounced grainy structure in the inner circle of the glow corresponding to the drop itself is inherent. Water samples from natural sources have higher biological indicators of the gas–discharge glow criteria. According to the results of the previously conducted experimental data, together with professor Kurikom M.V., in biological properties the most highly functional was monastic water. Figure shows examples of Kirlian images of different water samples.

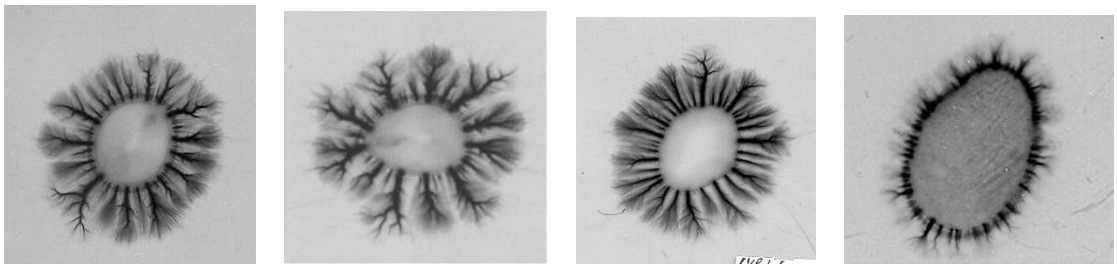

Figure. Kirlian images examples of various water samples

We conducted computer processing of Kirlian images of control samples of natural drinking water (CDW) before and after coherence. The results were compared with the magnitudes of the median and the difference between the parameters for experimental typal water developed by our early criteria for experimental typal water – distilled (type 1), plumbing (type 2), from natural drinking sources outside the territories of monasteries (type 3), from natural drinking sources on the territory of Kiev Pechersk Lavra (type 4). Degree of differences in the indicators was analyzed by the Euclidean distances for median values (EDM) and median differences (EDDM) when compared with each sample of typal water (TW 1–4).

The obtained results and their discussion. Table 1 presents the analysis results of brightness histograms for control and experimental samples of coherent drinking water for different coherence types and degrees.

Table 1

Data of brightness histograms for control and experimental samples of coherent drinking water for different coherence types and degrees

Water samples, pH	EDM 1 type	EDM 2 type	EDM 3 type	EDM 4 type	EDDM 1 type	EDDM 2 type	EDDM 3 type	EDDM 4 type
CDW(+1) pH 4,8	49125	54103	53974	45404	48127	53177	52370	47036
CDW (+2) pH 4,7	35131	33667	34661	33413	38316	38539	38740	39502
CDW (+3) pH 4,6	43717	50367	52534	41264	60884	67972	69808	56605
CHD (+1) pH 4,99	60565	58376	56928	58613	86096	81763	81309	88793
CHD (+2) pH 4,76	57203	54211	52714	55666	84356	79472	79137	87409
CHD (+3) pH 4,79	43953	51586	53270	40457	56581	64559	66147	51715
CDW (–1) pH 4,6	59904	69156	70951	56964	80328	88529	90449	74956
CDW (–2) pH 4,5	69146	71361	69267	67152	95668	95728	93303	97978
CDW (–3) pH 4,7	34597	37580	38233	31667	39799	44933	44567	38920
CHD (–1) pH 4,61	42313	43143	41353	41970	49435	49526	45320	54186
CHD (–2) pH 4.42	46163	50623	49530	43896	50899	53843	51524	52891
CHD (–3) pH 4,76	33351	35172	36126	33512	37595	41597	41200	38104

Note: EDM – Euclidian median, EDDM – Euclidian distance median difference, CDW– control water drinking, CHD – coherent water on drinking water, (+) – right–sided coherence polarization, (–) – left–sided, (1–3) – coherence degrees

To eliminate the effect of the initial characteristics of the control samples on the characteristics of coherent water samples, the values of the control samples were subtracted from the latter values, which is presented in Table 2.

Table 2

Differences between histogram indicators of DW control samples brightness and the corresponding samples of CHD of different degrees and polarization compared with typical water samples

The difference between the CDW and the CHD	pH	EDM 1 type	EDM 2 type	EDM 3 type	EDM 4 type	EDDM 1 type	EDDM 2 type	EDDM 3 type	EDDM 4 type
For +1	0,18	–11439	–4274	–2955	–13209	–37969	–28586	–28940	–41757
For +2	0,11	–22073	–20544	–18052	–22253	–46040	–40932	–40397	–47907
For +3	0,24	–236	–1219	–737	807	4304	3413	3661	4890

For –1	0,05	17592	26012	29599	14995	30892	39003	45128	20771
For –2	0,09	22983	20737	19736	23257	44769	41885	41779	45087
For –3	– 0,09	1247	2408	2107	–1844	2205	3335	3367	816

Note: the same

Table 3 presents data of comparative analysis of brightness histogram of control and experimental samples of CHD of both types with samples of typical water.

Table 3

Comparative analysis of EDM and EDDM brightness histogram of the control and experimental samples of CHD with samples of typical water

Samples	EDM 1 type	EDM 2 type	EDM 3 type	EDM 4 type	EDDM 1 type	EDDM 2 type	EDDM 3 type	EDDM 4 type
CDW (+1) and (+2)	13995	20435	19312	11990	9810	14638	13629	7535
CDW (+2) and (+3)	–8587	–16699	–17872	–7850	–22568	–29433	–31067	–17104
CDW (+1) and (+3)	5408	3736	1440	4140	–12758	–14795	–17438	7535
CHD (+1) and (+2)	3361	4165	4215	2946	1739	2292	2172	1385
CHD (+2) and (+3)	13250	2626	–557	15210	27776	14912	12991	35693
CHD (+1) and (+3)	56169	6791	3658	18156	29515	17204	15163	37078
CDW (–1) and (–2)	–9242	–2205	1685	–10188	–15341	–7198	–2854	–23021
CDW (–2) and (–3)	34549	33780	31034	35485	55869	50795	48736	59058
CDW (–1) and (–3)	25307	31575	32719	25297	40528	43597	45882	36037
CHD (–1) and (–2)	–3851	–7480	–8178	–1926	–1464	–4316	–6203	1295
CHD (–2) and (–3)	12813	15451	13405	10384	13305	12245	10324	14787
CHD (–1) and (–3)	8962	7971	5227	8458	11841	7929	4121	16082

The change in the degrees (+) coherence of natural drinking water in the magnitude of the EDM in comparison with TW 2 and TW 3 demonstrated similar trends among them, but different from TW 1 and TW 4. There are greater differences of all TW indicators in CHD (+2) and the smaller – in CHD (+3), compared with CHD (+2), but higher than of Water CHD (+1), the wave process is observed. Namely, compared with TW 2 and TW 3, as well as with TW 4, but changes in magnitude unlike TW 4 "delay". The latter is natural, because TW 4 water initially has ahighlyordered structure.

The difference in EDM in CHD indicators of dextrorotatory polarization with typal water at the 2nd degree is less than at the 1st degree. Large differences were when compared with tap water, which is explained as the most structurally different from other typical water as a result of technogenic effect. Smaller differences were when compared with monastic water (TW 4), as the

most structured and initially coherent. Moreover, the difference between the control samples was significantly higher in EDM with all kinds of typal water.

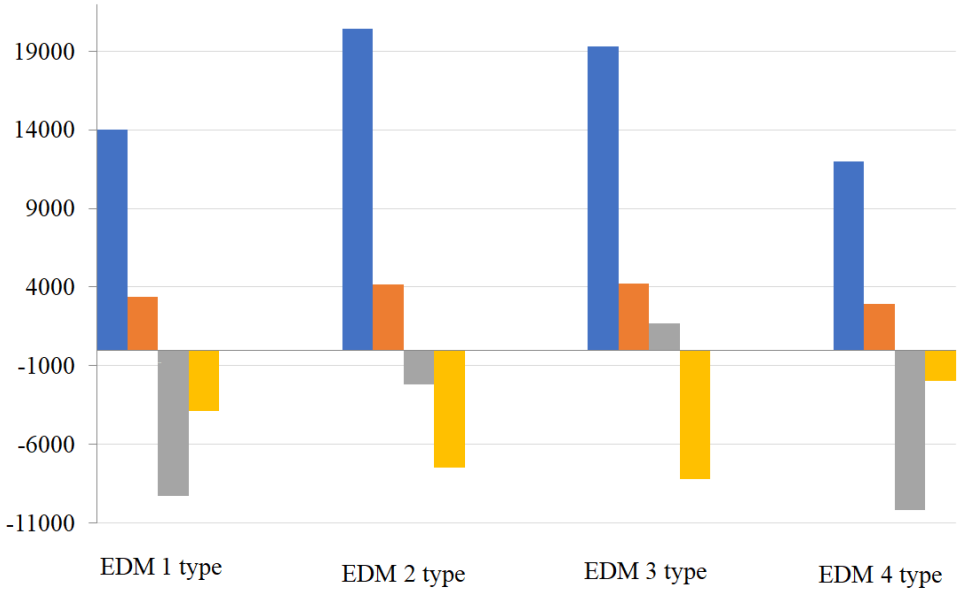

Chart 1. The indicators difference in the EDM control and experimental samples of CHD with typal water (1 column – between CDW (+1) and CDW (+2); 2 column – between CHD (+1) and CHD (+2); 3 column – between CDW (–1) and (–2); 4 column – between CHD (–1) and CHD (–2)

In contrast to the dextrorotatory (+) coherence of natural drinking water, with left–side (–) coherence, there is a clear increase in the differences from TW 2 (tap water) and TW 3 (natural) according to the degree of coherence and, less – from TW 1, minimally – from TW 4. At the same time, the control samples of them, on the contrary, were as different as possible on the EDM with the latter and slightly from TW 2 and TW 3.

Thus, the levorotatory coherence water prepared on natural drinking water, with the initially determined coherence, with a smaller (–) effect on it acquires properties, which more significantly distinguish it from the tap and typical natural water. At the same time, the 1st and 2nd degrees differ a little among themselves. Namely, having a smaller impact, it reveals quite stable other physical properties, as with (+) polarization. It changes in parameters of the latter, in contrast to changes in CHD samples (–), did not reveal the distinctiveness from more coherent TW monastic water.

With the 3rd degree (+) of coherence the differences from CHD (+2) revealed the same as in CHD (–2), the differences between monastery water from TW2 and TW3. Differences on EDM with TW between samples (–) CHD 2nd and 3–step degrees were insignificant. Between the samples of CHD (+2) and CHD (+3) were explicit withTW4, with the smallest differences from it. At the same time, in control samples of the CDW, the opposite patterns were observed in them, which demonstrates competence of the water coherence method.

When analyzing the EDM values between the samples of CHD (–2) and CHD (–3) with typal water, there was a decrease in differences with all typal water. They were 2 times more than among control samples. Water coherence changes them, making them more similar. Smaller differences between CHD (–3) and CHD (–2) were on the EDM with monastic water, but exceeded the difference between the parameters of CHD (–1) and CHD (–2). There is a step–by–step change in the physical properties of drinking natural water at both types of coherence, with a smaller interval at (–) polarization.

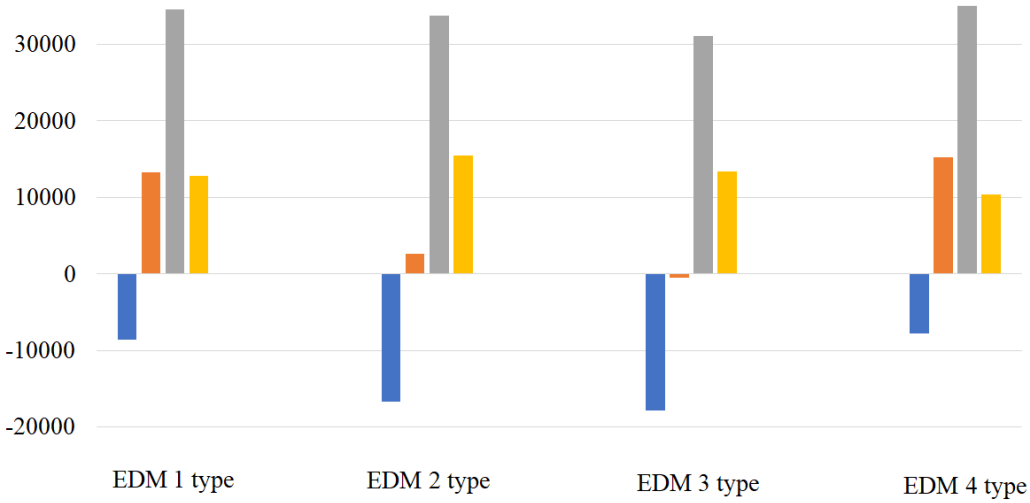

Diagram 2. The difference in indicators of the EDM of control and experimental samples of CHD with typal water (1 column – between CDW (+2) and CDW (+3); 2 column – between CHD (+2) and CHD (+3); 3 column – between CDW (–2) and (–3); 4 column – between CHD (–2) and CHD (–3)

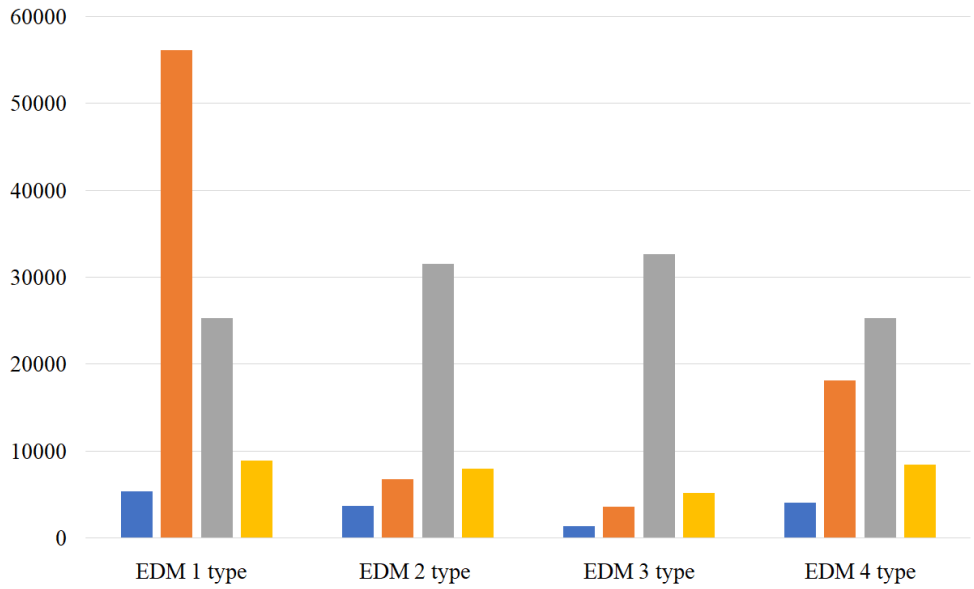

Diagram 3. Differences of indicators of the EDM of control and experimental samples of CHD with typal water (1 column – between CDW (+1) and CDW (+3); 2 column– between CHD (+1) and CHD (+3); 3 column– between CDW (–1) and (–3); 4 column – between CHD (–1) and CHD (–3)

As a result, while comparing the 1st and the 3rd degrees of samples (+) CHD of water, there are pronounced differences in their EDM with TW1 (distilled) and TW4 (monastic) water, compared with CHD (+2). Differences with TW1 –can be explained, since the distilled water is not coherent and during coherenization process it will differ less from the initial. CDW as initially having a certain coherence degree and polarity, already at (+) the 1st degree of coherence with our method, is easily rebuilt and acquired certain resistant electrophysical features that distinguish it from typical water 2 (tap water) and 3 (natural sources outside monasteries). With the 3rd degree of coherence, they are moderately and little differ from (+1) degrees, respectively. Control samples

of DW for these degrees of coherence are close to each other by moderate differences of their EDM with typal water.

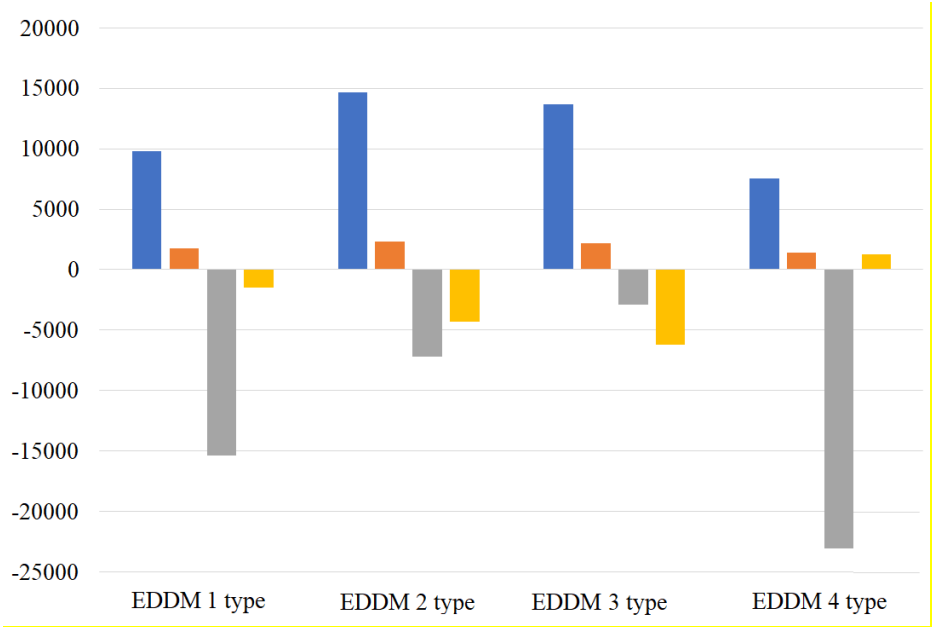

Diagram 4. Differences of EDDM indicators of control and experimental samples of CHD with typal water (1 column – between CDW (+1) and CDW (+2); 2 column – between CHD (+1) and CHD (+2); 3 column – between CDW (–1) and (–2); 4 column – between CHD (–1) and CHD (–2) (Table 3)

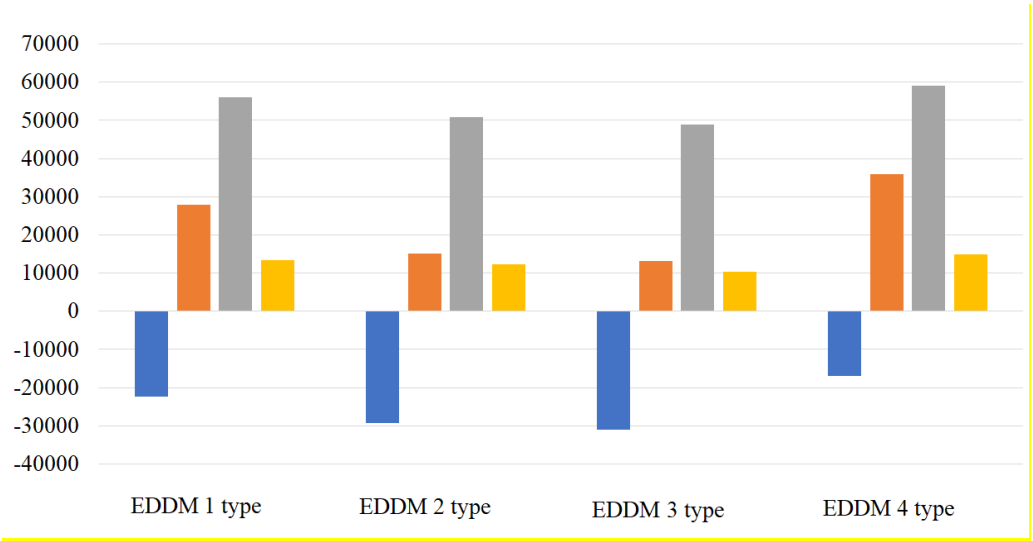

Diagram 5. Differences of EDDM indicators of control and experimental samples of CHD with typal water (1 column – between CDW (+2) and CDW (+3); 2 column – between CHD (+2) and CHD (+3); 3 column – between CDW (–2) and (–3); 4 column – between CHD (–2) and CHD (–3)

During levorotatory coherence as well as during (+) the smallest differences between the degrees were with respect to TW3 (natural sources outside monasteries). It is connected to a certain extent with preserving of natural water initial structural features. At the same time, at (–) coherence stable differences from the initial nature of DW and the approach to the monastic water was observed already at the 1st degree of coherence, while these differences decreased in the subsequent degrees. Differences from other TW were more demonstrative as compared with the

1st and 2nd degrees of CHD water. With (+) coherence, they are more pronounced when comparing the 1st and 2nd degrees of CHD water with the 3rd.

There are similar to EDM consistent patterns –are of minor differences, but smaller between EDDM indicators with all the TW between the samples of the 1st and 2nd degrees of CHD water. At (–) polarization in CHD (–2) water differences with TW 2 and TW 3 more than at CHD (–1), with TW 1 and TW 4 they are not significant.

From the data similar patterns were observed. They were obtained while analyzing the EDM values. In particular, the differences between the 2nd and 3rd degrees of CHD (+) in EDDM with TW1 and TW4 are pronounced. The differences in EDDM with TW 2 and TW 3 are 2 times less, which confirm the different structural and electrical properties of water from natural sources outside and on the monasteries territory. Differences of the values at (–) coherence between the 2nd and 3rd degrees of typal water, as well as of EDM, were less demonstrative. Also we revealed parameters differences in the samples of the control water taken from one source.

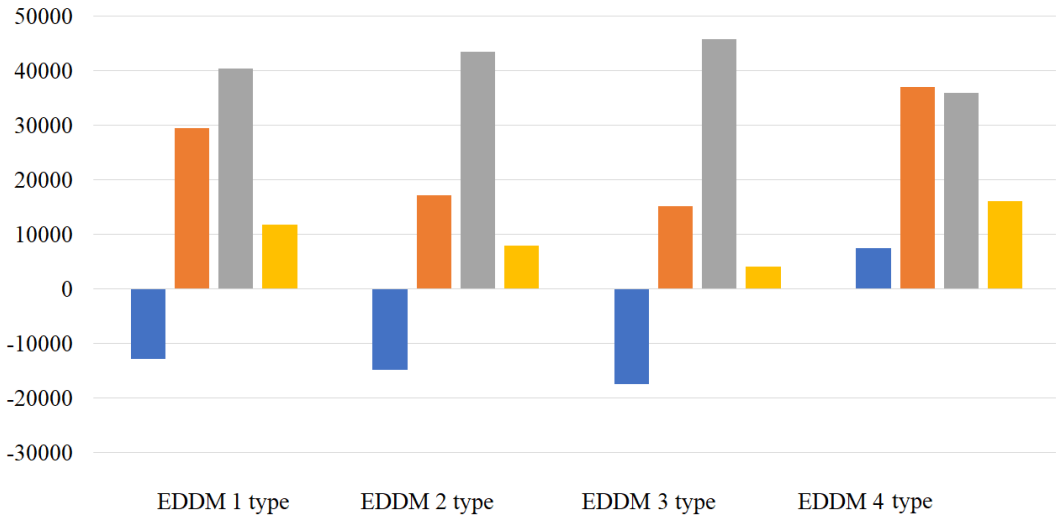

Diagram 6. Differences of EDDM indicators of the control and experimental samples of CHD with typal water (1 column – between CDW (+1) and CDW (+3); 2 of column – between CHD (+1) and CHD (+3); 3column – between CDW (–1) and (–3); 4 column – between CHD (–1) and CHD (–3).

As in the ECM indicators, there are significant differences on the comparative analysis diagram of EDDM during the (+)of drinking water between the 1st and 3rd degree with typical TW 1 and TW 4 samples and two fewer differences with TW 2 and TW 3. The differences between natural and monastic monastery are discovered again. At (–) coherenceof CDW, as well as according to the results of EDM, the differences in degrees were the smallest with TW 3. However, in EDDM, we obviously observe the maximum differences with TW 4, compared with the less pronounced on EDM. Thus, when assessing the type and degree of water coherence, it is necessary to analyze both parameters of the brightness histogram of Kirlian photography of water.

Also, as in EDM, with (+) coherence, more explicit differences between the quantities were observed when compared with the 1st and 2nd degrees of CHD of water with the 3rd one. At (–) coherence, the resistant magnitudes approximation to monastic water was observed at the 1st degree of coherence, with the differences decrease in the subsequent degrees. Differences from other TW were more demonstrative also when compared with the 1st and 2nd degrees of CHD water at (–) polarization and the 1st and 2nd degrees of CHD of water with the 3rd one.

Conclusion

1. Kirlian photography of water is a rather informative method for evaluating its electrophysical properties.

2. Method of computer analysis of the Kirlian images, applied by us for allocation of 4 classes of typal water, characterized by the coherence degree, with the highest coherence degree from monastic sources, can be used as an express method to estimate coherence of water prototypes.

3. In the research of the electrophysical water properties, a comparative analysis with control water samples is necessary, including water sampleswhich were taken from one water source.

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CHAPTER 5. EFFICIENCY OF LONG-TERM PASSIVE THERAPY FOR RECOVERY OF LIMB FUNCTION AFTER TOTAL KNEE ARTHROPLASTY

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Abstract. *Total knee arthroplasty is considered a radical and effective method of treating osteoarthritis of the knee.The meta-analysis of scientific researches regarding the efficiency of long-term rehabilitation after total knee arthroplasty is carried out and supplemented. The complex program for physical rehabilitation in combination with the Artromot Active-K device in the long-term rehabilitation period after total knee arthroplasty is proposed. The effectiveness of the developed set of physical exercises in combination with apparatus methodology and their use in restoring the functions of the limb after endoprosthetics, which significantly reduces the intensity of pain, increases of the knee joint mobility, expands the motor mode of patients, is proved in practice. The results of the scientific researchare of great practical importance for the improvement of the long-term rehabilitation system for persons after total knee arthroplasty.*

Key words: *osteoarthritis, gonarthrosis, knee joint, total knee arthroplasty, physical rehabilitation, physiotherapy exercises.*

Introduction

The knee joint (KJ) in everyday life experiences enormous stress, most often several times the body weight. Such an excessive strain per unit area of the articular cartilage is a strong negative factor resulting in its degeneration. When descending the stairs in the KJ on the top line, the peak strain on the articular cartilage reaches 346% of the body weight, when climbing stairs – 316%, when getting up from a chair – 246%, when sitting on a chair – 225%, when standing on one leg – 259%, when standing on two legs, the effect on the cartilage of the joint is 7% more than the body weight [1].

Gonarthrosis (deforming arthrosis, osteoarthrosis (OA), osteoarthritis, degenerative arthritis) is a polyetiological degenerative-dystrophic disease of the KJ, characterized by damage to the hyaline cartilage, followed by the formation of osteocartilaginous growths, deformation. Disintegration of joint cartilage is the main pathological manifestation of OA. Along with the destruction of articular cartilage in case of degenerative-dystrophic diseases, other components of the joint are also involved: subchondral bones, synovial membrane, joint ligaments and capsule, periarticular muscles. OA, also known as degenerative articular disease of the joints, is usually a result of wear and tear and possible loss of articular cartilage. More common of older women and men [7].

Arthrosis of the KJ can be divided into two types, primary and secondary. Primary osteoarthrosis is joint degeneration for no apparent underlying reason. Secondary osteoarthrosis is a consequence of either an abnormal concentration of force in the joint, both for post-traumatic reasons, and abnormal articular cartilage, such as rheumatoid arthritis (RA). Osteoarthrosis is usually a progressive disease that can result in disability over time. The intensity of clinical symptoms may differ from person to person. However, they become more severe, more frequent and debilitating over time. The rate of progression also varies for each person. Common clinical symptoms include knee pain that gradually begins and increases when moving, stiffness and swelling of the knee, pain after prolonged sitting or rest, and increasing pain over time [9].

Osteoarthrosis of the KJ accounts for 24.7 to 54.5% of diseases of large joints. The progression of degenerative-dystrophic diseases of the KJ within 12-15 years results in disability often even of working age. Osteoarthrosis of the KJ in 10-21% of cases causes a decrease in working capacity and disability. Disabled is 1 in 100 patients suffering from diseases of the locomotorium; the most severe course is characterized by KJ osteoarthrosis. A significant decrease in the quality of life of disabled persons is associated with joint pain, reduced mobility and loss of the ability to look after themselves [4].

The main reason for the development of OA is an imbalance of the processes of destruction of cartilage and its recovery due to various endogenous and exogenous factors, such as joint injury, ratio distortion of surfaces as a result of congenital, traumatic reasons; metabolic and endocrine disorders, overweight. As a result, the normal strain becomes excessive and causes degeneration of the articular cartilage, resulting in deforming arthrosis and aseptic joint inflammation. Inflammatory processes of an infectious and non-communicable nature, dystrophy of the KJ and soft tissues, regenerative tissue changes, hereditary diseases, trauma may be the reason of KJ diseases [6].

Clinical symptoms of KJ can be: pain syndrome, soft tissue edema, deformation of the KJ, crackle when bending, local temperature increase, reduced mobility of the KJ. Despite the level of development of science in the world, medicine is not able to solve the main issue of orthopedics – the recovery of the affected articular cartilage. Basically, all the conservative measures are aimed at temporary pain relief only. When pain and functional disability cease to be resistant, the final method of treatment is total knee arthroplasty (TKA), which allows to stop pain syndrome in the shortest possible time, reproduce the limb axis and restore the lost function of the KJ [8].

Total knee arthroplasty is considered to be a radical and effective method of treatment of osteoarthrosis of KJ. Despite the accumulated extensive experience of TKA, continuous improvement of endoprostheses, tools and techniques for their implantation, complications arise in 3-15% of patients at different times after the surgery. Among them are superficial and deep suppuration (0.2-9%), aseptic loosening of the components of the endoprosthesis (8-22.2%) [5]. However, there are no clear rules for physical rehabilitation after TKA at present, that is why the issue of studying TKA is relevant.

The purpose of the study. To develop and practically substantiate an increase in the effectiveness of passive therapy after total knee arthroplasty in the long-term postoperative period of rehabilitation.

Material and methods of research

To accomplish the assigned tasks, the following research methods have been used:

- Sociological research method – questioning;
- Medical and biological research methods;
- Statistical methods.

To conduct a questionnaire to assess the patient's quality of life, the MOS SF-36 questionnaire – Health Questionnaire – 36 was used. This questionnaire has been developed in the USA and contains 8 scales and 36 questions. It allows you to assess the overall health of the patient. And indicates the level of physical and mental state, as well as social functioning.

Biomedical research methods of patients before and after rehabilitation treatment are carried out by using International tests. To characterize the pain syndrome and the functional state of the KJ, the International Knee Assessment Scale was used [11]. The scale contains 6 points, where the normal indicator is 100 points, and in the presence of osteoarthrosis – 0 points. The quantitative assessment of pain experience is performed by the patient himself by using the visual analogue scale (VAS) [12].

The VAS is designed to determine the patient's subjective pain sensation at the time of the study. This scale can be used to determine the dynamics of pain intensity over 24 hours or 1 week. However, it should be borne in mind that memories of pain can be inaccurate and often distorted under the influence of other circumstances. VAS is a horizontal line 10 cm long with the inscription under the left edge "No pain", which means 0 points, and under the right - "Worst pain imaginable",

which means 100 points. The segment within the first 4 cm corresponds to the lack of pain, 5-44 mm – mild pain, 45-74 mm – moderate pain, 75-100 mm – severe pain. The patient should draw a vertical line across the indicated line in the place most appropriate to the intensity of pain at the time of examination. The advantage of VAS is its availability for statistical processing. The systematic measurement of pain by using the VAS gives a pattern of the dynamics of pain and the effectiveness of treatment.

Overall knee function was assessed by using the Oxford Knee Scale [10]. This scale consists of 12 points and allows the patient to characterize pain sensations, as well as to perform daily various activities. The dynamics of the functional state of the joints was assessed by using the WOMAC index (Osteoarthrosis Index of the University of Western Ontario and McMasters). The WOMAC scale includes 24 questions in 3 sections. The patient, answering the questions, chooses the answers that best describe his condition in points: from 0 to 100. An increase in the total number of points indicates a deterioration in the functional state of the KJ. To study the locomotor function of the KJ, the time (in seconds) was determined where the patient had to travel 15 m at the maximum pace.

For statistical analysis and modeling, a personal computer with an Intel Core2Quad processor with 4 GB of RAM in the standard configuration was used. To organize and form a matrix of data, tables and graphs, MS Office 2010 was used. The probability of data was determined by using the method of mathematical statistics by the Student's t-criterion.

The study was carried out from November 2019 to March 2021 on the basis of the rehabilitation treatment department of the Medical Center of the Karpaty State Medical Center in the town of Truskavets. The involvement of patients in the experiment was carried out as they entered physical rehabilitation on the 5-10th day after discharge from the hospital. The group consisted of 18 patients who underwent TKA at the age of 35 to 65 years (48.28 ± 2.89) with a diagnosis of osteoarthrosis of the KJ. The main selection criteria for the patients who took part in the study were the following: the lack of general contraindications to physical rehabilitation and their voluntary consent. The patients were divided into two groups: the control group – 10 (50.20 ± 2.81) and the main group – 8 patients (45.88 ± 3.37).

The rehabilitation process of the control group was carried out according to the standard physical rehabilitation program adopted in the treatment center:

- physiotherapy procedures: acupuncture, electrophoresis, muscle electrical stimulation, balneotherapy;
- therapeutic massage;
- nutritional correction to reduce the excess body weight of patients;
- a set of therapeutic exercises according to the methodology used in the medical institution.

The duration of rehabilitation of patients in two groups was 21 days [3]. The main group included the use of passive movement therapy by using the Artromot Active-K apparatus for a long period of time in addition to the above-described exercises [2]. The device is based on the method of motor passive therapy (CPM – therapy (Continues Passive Motion)). This method allows you to perform passive movements with the diseased joint. Exercises performed by the patient on the device do not cause painful sensations. During a mechanotherapy session, the KJ performs rhythmic passive movements, where, as a result of the procedures performed, edema decreases, blood circulation improves and pain is eliminated. All patients at the beginning of rehabilitation and at the end of rehabilitation treatment conducted a questionnaire to assess the quality of life. The data obtained during the initial questionnaire survey and testing of both groups were compared to assess the effectiveness of the proposed method of KJ rehabilitation in the postoperative rehabilitation period.

Results of research and their discussion

As a result of the performed rehabilitation, one can see the dynamics of updating the indicators of the functional state of the operated limb of patients of the main and control groups. It should be noted that after the completion of the planned course of rehabilitation, patients of both groups showed positive changes in almost all parameters assessing the functional state of the KJ:

an increased mobility of the operated joint and muscle strength, return of the correct walking stereotype on flat and uneven terrain, on the stairs.

The quality of life was assessed according to the "MOS SF-36" - "Health questionnaires – 36" research method. The questionnaire determines the assessment of the quality of life in the preoperative period at the beginning of the rehabilitation course and one month after its completion of 8 patients who underwent a course of recovery physiotherapy according to the method of therapeutic physical training developed by us, as well as 10 patients in the control group. The data are presented in Table 1.

Table 1

The main parameters of the quality of life of patients after TKA before and after rehabilitation

Parameter name	Quality of life parameters before rehabilitation		Quality of life parameters after rehabilitation	
	main group	control group	main group	control group
Overall health	13,7±1,6	15,6±0,9	22,7±1,4*	18,4±1,9
Physical functioning	14,5±1,8	16,1±0,8	24,2±1,5*	20,4±1,6**
Role physical functioning	4,3 ±0,7	5,2 ±0,8	5,7±0,6*	4,6±0,9**
Pain scale	4,8±0,7	6,8±0,7	4,2±0,2*	6,2±0,4
Viability	14,7±0,3	16,1±0,8	21,6±0,6*	17,7±0,8**
Social functioning	6,8±0,5	5,5±0,5	2,7±0,2*	4,8±0,5**
Role emotional functioning	5,1±0,3	3,6±0,1	5,6±0,2	4,2±0,3**
Mental health	15,6±0,7	14,9±0,8	25,7±0,5*	18,2±1,1**

Note * - significant differences in indicators before and after rehabilitation within the group ($p < 0.05$); ** - significant differences in indicators in the main and control groups after rehabilitation ($p < 0.05$).

According to the results of the table, before undergoing rehabilitation of the examined patients, all the parameters of both groups on the quality-of-life scales were reduced and amounted to: 4.8 ± 0.7 in the main group; 6.8 ± 0.7 in the control group before rehabilitation and 4.2 ± 0.2 and 6.2 ± 0.4 after rehabilitation according to the pain scale. It is obvious that pain syndrome, which is the main parameter in case of gonarthrosis and after arthroplasty, results in a decrease in physical functioning, the parameters of which were as follows: 14.5 ± 1.8 in the main group, 16.1 ± 0.8 in the control group before rehabilitation, and 24.2 ± 1.5 in the main group, 20.4 ± 1.6 in the control group after rehabilitation – according to the scale of physical functioning. A decrease in the indicator of the parameter of physical functioning is associated with the limitation of daily and professional activities depending on the handicap, namely the deterioration in the quality of life according to the scale of role physical functioning, the indicators of which were: 4.3 ± 0.7 in the main group, 5.2 ± 0, 8 in the control group before rehabilitation and 5.7 ± 0.6 in the main group, 4.6 ± 0.9 in the control group after rehabilitation; social factor of functioning, the parameters of which, according to the scale, corresponded to the following indicators: 6.8 ± 0.5 in the main group, 5.5 ± 0.5 in the control group before rehabilitation and 2.7 ± 0.2 in the main group, 4.8 ± 0.5 in the control group after rehabilitation.

Decrease in indicators on the scales of role emotional functioning (5.1 ± 0.3 in the main group, 3.6 ± 0.1 in the control group before rehabilitation and 5.6 ± 0.2 in the main group, 4.2 ± 0.3 in the control group after rehabilitation and viability (14.7 ± 0.3 in the main group, 16.1 ± 0.8 in the control group before rehabilitation and 21.6 ± 0.6 in the main group, 17.7 ± 0.8 in the control group after rehabilitation is the result of negative emotions and anxiety, which is clearly illustrated on the scale

of the mental state and is expressed by a decrease in its indicators: 15.6 ± 0.7 in the main group, 14.9 ± 0.8 in the control group before rehabilitation and 25 , 7 ± 0.5 in the main group (18.2 ± 1.1 in the control group after rehabilitation) As a result of changes in mental and physical health, a decrease in the parameter of general health occurs (13.7 ± 1.6 in the main group, 15, 6 ± 0.9 in the control group before rehabilitation and 22.7 ± 1.4 in the main group, 18.9 ± 1.9 in the control group after rehabilitation).

Changes in the parameters of the quality of life after undergoing rehabilitation of patients of the main group indicates a significant positive effect of the program of rehabilitation measures on the main components of the quality of life, namely, on the factor that has been eliminated as a result of arthroplasty and due to physical rehabilitation. In fact, this has resulted in an increase in the patient's self-esteem on the scales of physical and role functioning. According to the parameters of the scales of role emotional functioning, vitality and social functioning, an increase in indicators is obvious, explained by a surge of positive emotions as a consequence of the result obtained. But, the indicators on the scales of overall health, physical and role-based physical functioning are not high, since patients still cannot move and work on their own. At the same time, they objectively assess their state of health and possible prospects for the future, which is manifested in a low assessment of overall health.

In general, we can talk about the improvement of all the studied parameters of the quality of life after the completion of the physiotherapy program of patients of both the control and the main groups, especially when compared with the parameters of the quality of life after discharge from the hospital. Reliable results of improvement of the main group in comparison with the control group were obtained for all parameters of the quality of life. Consequently, the analysis of the quality of life of patients after TKA showed a decrease in the indicators of the quality of life in the pre-rehabilitation period and a significant recovery after the rehabilitation program in the late post-rehabilitation period.

The parameters for assessing the KJ were determined according to the International Knee Assessment Scale [11]. The dynamics of the study of knee arthroplasty patients showed that the parameters of the KJ assessment scale change depending on the rehabilitation in both groups, although to a different extent of significance and manifestation. The patients of the main group have a clearly pronounced tendency towards the improvement. The value of the KJ assessment scale increased by 33.4 points (from 42.38 ± 1.47 to 75.8 ± 6.9). The control group also differed in an improvements in indicators by 14.4 points (from 40.2 ± 1.39 to 54.6 ± 1.57) (Table 2).

Table 2

Dynamics of indicators of the KJ scale (points) after total arthroplasty

Groups	Before rehabilitation	After rehabilitation
Main	42,38± 1,47	75,8 ± 6,9*
control	40,2 ±1,39	54,6 ±1,57* **

Note * - significant differences in indicators before and after rehabilitation within the group ($p < 0.05$); ** - significant differences in indicators in the main and control groups after rehabilitation ($p < 0.05$).

A combined visual analogue pain scale (VAS) was used to assess the effectiveness of the proposed physiotherapy procedures and quantitatively assess the pain syndrome of patients of both groups before and after the course of physiotherapy. The dynamics of the study of total knee arthroplasty patients showed that the parameters of the pain scale change as a result of physiotherapy in both the main and control groups, but with different indicators of significance and manifestation. Under the influence of a specially developed program of physical exercises of therapeutic physical training, a statistically significant positive result of a decrease in the pain factor in the main group by 2.39 points (5.71 ± 0.11 to 3.32 ± 0.08) was obtained; the control group

also revealed an improvement: the parameters of the pain scale decreased by 3.78 points (6.16 ± 0.07 to 3.94 ± 0.06) (Table 3).

Table 3

Dynamics of VAS parameters

VAS scale parameters		Before rehabilitation (points)	After rehabilitation (points)
groups	Main	5,75 ± 0,52	3,38 ± 0,35*
	control	6,20 ± 0,34	3,90 ± 0,40*

Note * - significant differences in indicators before and after rehabilitation within the group ($p < 0.05$).

The general functional activity of the KJ after the total arthroplasty was assessed by using the Oxford scale. To determine the effectiveness of the proposed therapeutic physical training complex with the predominant influence of the use of physical exercises of patients of both groups, before and after a course of physiotherapy, the general function of the KJ was determined by using the Oxford scale for the KJ [10]. The dynamics of examination of patients after total knee arthroplasty showed that the parameters of the Oxford scale change as a result of physiotherapy in both the main and control groups, but with different indicators (Table 4).

Table 4

Dynamics of the Oxford Scale parameters after total knee arthroplasty

Indicators of the Oxford Knee Scale		Before rehabilitation (points)	After rehabilitation (points)
Groups	Main	34,13 ± 1,71	42,38 ± 1,47*
	control	30,40 ± 2,1	34,4 ± 1,54 **

Note * - significant differences in indicators before and after rehabilitation within the group ($p < 0.05$); ** - significant differences in indicators in the main and control groups after rehabilitation ($p < 0.05$).

Statistically accurate values of the parameter's improvement were observed after the completion of the rehabilitation course in the main group. The indicators of the Oxford scale changed of patients of this group by 8.2 points (from 34.13 ± 1.71 to 42.38 ± 1.47). The control group also showed an improvement by 4 points (from 30.40 ± 2.1 to 34.4 ± 1.54).

Dynamic indicators of the functional state of the KJ were assessed by using the WOMAC index. To analyze the dynamics of the main functions after total knee arthroplasty, it is shown in Table 5, which shows the total normalized value of the / WOMAC index in the study and control groups of patients. Significant positive dynamics of the patients of the main group under the influence of a special therapeutic physical training program was observed. The value of the index / WOMAC decreased in this group on the pain scale by 49%; on the morning stiffness scale by 59%; on the scale of joint physical function by 31% and the normalized value of the index by 37%. The indicators of patients of the control group under the influence of the standard complex of therapeutic physical training were lower and amounted to: 38%, 44%, 21%, 27%, respectively (Table 5).

To determine the locomotor function of the KJ after total arthroplasty, the time required for patients to travel 15 m at the maximum pace before and after physiotherapy was researched. Examination of patients showed that the test indicators change during treatment in both groups, but if in the main group we see a statistically important improvement after treatment using the developed therapeutic physical training program – a decrease in the travel time by 9.8 s (from 30.7

± 1.7 to 20.9 ± 1.2), then the speed of movement of patients in the control group changed less: the travel time decreased by 5.1 s (from 29.4 ± 0.9 to 24.3 ± 0.8).

Table 5

Dynamics of the index / WOMAC indicators under the influence of rehabilitation

Functional Index / WOMAC	Groups					
	main			control		
	Before rehabilitation	After rehabilitation	% Decrease	Before rehabilitation	After rehabilitation	% Decrease
Pain scale (points)	421,2± 11,5	213,13± 21,2*	49%	445,9± 17,7	279,9 ± 29,5**	38%
Morning stiffness scale (points)	144,2± 14,3	59,6± 9,4*	59%	134,2± 8,1	75,8± 6,9	44%
Joint physical function scale (points)	1243,8± 22,2	867,8± 23,4*	31%	1123,4± 24,9	895,4± 26,2	21%
Normalized WOMAC index value (points)	1809,4± 29,1	1142,6± 30,3*	37%	1705,6± 33,6	1251,7± 36,4**	27%

Note * - significant differences in indicators before and after rehabilitation within the group ($p < 0.05$); ** - significant differences in indicators in the main and control groups after rehabilitation ($p < 0.05$).

Conclusions

As a result of the rehabilitation, the dynamics of recovery of indicators of the functional state of the operated limb is observed of the patients of main and control groups. It should be noted that after the completion of the planned course of rehabilitation, patients of both groups showed positive changes in almost all the parameters assessing the functional state of the knee joint: an improved mobility of the operated joint and muscle strength, the return of the correct walking stereotype on flat and uneven terrain, on the stairs, but with different extent of manifestation.

Under the influence of a specially developed program of therapeutic physical training, a statistically accurate positive result of a decrease in the pain factor in the main group by 2.39 points (5.71 ± 0.11 to 3.32 ± 0.08) was obtained; an improvement was also observed in the control group: the parameters of the pain scale decreased by 3.78 points (6.16 ± 0.07 to 3.94 ± 0.06).

Statistically accurate values of the parameter's improvement were observed after the completion of the rehabilitation course in the main group. The indicators of the Oxford scale changed of patients of this group by 8.2 points (from 34.13 ± 1.71 to 42.38 ± 1.47). The control group also showed an improvement by 4 points (from 30.40 ± 2.1 to 34.4 ± 1.54).

The dynamics of the study of knee arthroplasty patients showed that the parameters of the knee joint assessment scale change depending on the rehabilitation in both groups, but with different extent of significance and manifestation. The patients of the main group showed a clear pronounced tendency towards the improvement. The value of the knee joint assessment scale increased by 33.4 points (from 42.38 ± 1.47 to 75.8 ± 6.9). The control group also differed in the improvement in the indicators by 14.4 points from 40.2 ± 1.39 to 54.6 ± 1.57.

To determine the locomotor function of the knee joint after total arthroplasty, the time required for patients to travel 15 m at the maximum pace before and after physiotherapy was studied. Examination of patients showed that the test indicators change during treatment in both groups, but if in the main group we see a statistically important improvement after rehabilitation by using the developed therapeutic physical training program – a decrease in the travel time by 9.8

s (from 30, 7 ± 1.7 to 20.9 ± 1.2), then the speed of movement of patients in the control group changed less: the travel time decreased by 5.1 s (from 29.4 ± 0.9 to 24.3 ± 0.8).

The results of the overall assessment of the effectiveness of rehabilitation of patients showed that of patients of the main group, under the influence of a special program of long-term therapy and the apparatus method, a significant positive dynamics was observed. The value of the index indicators on the WOMAC scale decreased in this group on the pain scale by 49%; on the morning stiffness scale by 59%; on the scale of joint physical function by 31% and the normalized value of the index by 37%. The indicators of patients of the control group under the influence of the standard complex of rehabilitation were lower and amounted to: 38%, 44%, 21%, 27%, respectively.

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