

SECTION 2. INNOVATION

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2.1 Innovations of veterinary reproductology in collaboration with related sciences

Veterinary support of animal reproduction is one of the most science-intensive directions and currently has a significant arsenal of tools [188-190]. However, the request for practice prompts the development of reliable, fast, and affordable, innovative solutions to improve the possibility of early diagnosis, prevention, and therapy of disorders of the reproductive function of animals, objectification, and improvement of their effectiveness [191-195].

Thus, the diagnosis of disorders of reproductive function is somewhat problematic even in humane medicine with the use of state-of-the-art scientific achievements. At the same time, significant morphological and functional changes in sexual organs regulating reproductive function can be numerous and diverse. Therefore, the final stage of diagnosis requires a systematic analysis of all the received data and a methodical, scientifically based approach to this issue with the involvement of modern science and technology assets. Using the latest achievements in the sciences related to reproduction is also relevant to develop preventive or curative measures [190].

The latest achievements in diagnosing the condition of organs and systems and developing pathologies are associated with the introduction of the ultrasound method. Thanks to echography with three-dimensional image reconstruction, echocardiography, Doppler echocardiography, and dopplerometry with color Doppler mapping, the accuracy of diagnosis of anatomically expressed anomalies of fetal development increases significantly. In addition, it allows to study of the peculiarities of the development of the embryo, fetus, and placenta during an uncomplicated pregnancy, to predict the course of gestation and the possible formation of deviations from its ordinary course. Accordingly, the use of complex differentiated therapy for pregnancy complications allows for a significantly reduced frequency of the threat of

termination of pregnancy, placental insufficiency, reduced the frequency of perinatal losses due to the reduction of ante- and intranatal mortality [196, 197].

A place has been found for the introduction of thermography (infrared thermography, thermal imaging, thermal imaging, or thermal video) – a method of recording infrared radiation of anybody with special susceptible devices (thermal imagers), the temperature of which is above absolute zero [198]. Thermographic cameras detect radiation in the infrared range of the electromagnetic spectrum (approximately 0.9-14 microns) and create images that identify overheated or hypothermic places based on this radiation. Since all objects with temperature are capable of infrared radiation, according to Planck's formula for blackbody radiation, thermography allows to "see" the environment with or without visible light. The intensity of thermal radiation of the body increases as its temperature increases, so thermography allows to see the temperature distribution on the body surface [199].

Thermography is a promising non-contact remote-diagnostic express method of obtaining a thermogram (an image in infrared rays showing a pattern of temperature field distribution). Being a harmless and objective examination method, it allows the detection of differences in the distribution and intensity of infrared radiation depending on the physiological or pathological state of the animal's body. In particular, it provides detection and differentiation of sexual cycle phenomena; determination of the degree of androgenesis and spermatogenesis, diagnosis of pregnancy; preventive diagnosis of pathological processes at the preclinical stage of development; detection of pathologies, the genesis of which lies in dystrophic or inflammatory processes; assessment of the therapeutic effect [192].

Preventive diagnostics of sexual cycle phenomena using thermal imaging can be used for females of various species of animals. The obtained information is confirmed by other research methods with mandatory elements of differentiation. Temperature fluctuations of the external genitalia depend on the phenomena and are recorded thermoscopically. Thus, in animals during estrus, the temperature of the external genital organs is higher than during diestrus. At the same time, the external genitalia is characterized by large areas of "hot" colors of the palette; in the case of an adverse

reaction (absence of the arousal stage of the sexual cycle), the temperature of the external genitalia almost does not differ from the temperature of the surrounding tissues. The results of the research reliably confirm the regularity of the increase in the temperature of the external genital organs during the arousal stage of the sexual cycle, which allows remotely (contactless) receive the necessary information about the condition of the animal in general and, in particular, its external genital organs.

Preventive diagnosis of pregnancy using thermal imaging. The temperature gradient of the external genitalia of pregnant females is low, and the thermogram of the external genitalia is represented by the "warm" colors of the palette.

Remote determination of the morpho-functional state and weight of newborns using thermal imagers. In the case of normotrophs, the temperature curve is insignificant, and the intensity of the red "hot" color on the thermogram is relatively evenly distributed throughout the body, which indicates the completeness of thermoregulation in typically developed neonatal animals. When studying hypotrophs, a completely different picture is observed: the head is much warmer than other parts of the body - the back part is less supplied with blood, is cooler, and therefore has a yellow color with a transition to green. This indicates that the formation of thermoregulation is at a low level; such animals need additional heating, spend extra calories on their inefficient heating and significantly reduce daily gains.

Using a thermal imager makes it possible to remotely determine the general and local temperature of the nest, the measurements and weight of piglets and rabbits, and the milk yield of sows and rabbits. Analysis of thermograms allows for establishing hypothermia and hypotrophy of piglets in the early stages of the postnatal period and diagnosing some diseases, such as antenatal hypotrophy and those accompanied by local hyperthermia. Implementing this method makes it possible to significantly reduce human and economic resources in diagnosing pathologies of the postnatal period, adjusting the conditions of keeping newborns, and predicting their further development.

Determination of the functional state and preventive diagnosis of pathological processes in the genitals using thermal imaging. During the thermographic study of

females, the dependence of the temperature gradients of the external genitalia on the morpho-functional state of the ovaries is noted. At the same time, females with hypogonadism have a lower temperature gradient than animals with normal ovaries. Thermograms of the external genitalia of females with full sexual function is characterized by a predominance of "warm" colors of the palette (red and orange); in animals with hypogonadism, on the contrary, "cold" colors (blue and green) prevail. In addition, the thermograms of the genital organs of females with hypogonadism are characterized by pronounced thermal asymmetry and thermal spotting of the studied area, which are characteristic signs of blood circulation disorders.

The characteristics of thermoscopic and thermographic indicators of the external genitalia of females with hypoluteolysis are similar to those of hypogonadism. That is, a decrease in the temperature gradient and a predominance of "cold" colors in the palette are recorded.

According to thermoscopic studies of females with cystic degeneration of ovarian follicles, a sufficiently long increase in the temperature gradient of the external genitalia is noted. Thermograms of the genitals of such animals are characterized by "hot" colors on the palette.

With vestibulovaginitis, the temperature gradient increases, and thermograms are characterized by hot colors of the palette of the organ under study.

The thermogram of the external genitalia of females with metritis is characterized by intensely "hot" colors of the palette, which are evenly registered on the examined organ. The presence of secretions from the external genitalia can also be observed on thermograms. These highlights are usually presented in the form of "cold" (blue and green shades) colors of the palette. In a detailed study, inflammatory exudate is differentiated from estrous mucus.

Such research results confirm the regularity of temperature increase during inflammatory processes, which can be determined remotely using thermal imaging technology.

During the thermoscopic examination, the dependence of temperature gradients of testicles on their morphofunctional state is noted in males. At the same time, the

temperature gradient in animals with dystrophy and hypogonadism is lower compared to a full-fledged reproductive function. The predominance of "warm" colors in the palette (red and orange) is characteristic of the thermograms of the testicles of males with total reproductive capacity. While thermographic images of testicles of animals with testodystrophy and hypogonadism were characterized by pronounced thermospotting of the studied area, and the predominance of "cold" colors is typical for blood circulation disorders.

With orchitis, there is an increase in the size of the testicles and a decrease in the echogenicity of the parenchyma while maintaining homogeneity. Tissue swelling is manifested by a decrease in echogenicity and thickening in the area of the muscle-elastic membrane.

Males with balanoposthitis have a pronounced zone of hyperthermia, and "hot" palette colors prevail [192].

The developed therapy methods and prevention of reproductive pathologies involve using original drugs. They aim to normalize homeostasis, restore the morphofunctional state of regulatory organs, and perform sexual function [190].

Current conditions of practical veterinary medicine require effective and safe drugs. Biotechnological methods in the management of reproduction should serve the maximum use of the reproductive potential of animals, subject to deep knowledge and observance of the biological laws of reproduction and the use of these methods in animals with optimal health and physical condition. In particular, such an essential technological stage of animal husbandry as reproduction involves the use of hormonal drugs. However, when using this or that hormonal drug, it should be borne in mind that its effect on the female reproductive system may manifest differently depending on the functional state of the reproductive organs and the body's hormonal status. Incorrect, without considering the indications, the introduction of the drug can have negative consequences. Although not all researchers share this point of view and have not established an adverse effect of even repeated use of hormonal drugs on sexual function, which should be related to optimizing the doses of the drugs used.

Along with the already known and used drugs, it is necessary to search for new drugs that are harmless to the body and have a physiological focus of action. Recently, attention has been paid to herbal preparations in both human and veterinary medicine. Many plants contain biologically active substances, among which phytohormones deserve special attention, which is relevant and logical for the practice of reproductive veterinary medicine. The spectrum of action of these substances is vast (phytoestrogens, antiestrogens, antigonadotropins), which allows them to be used for treating animals with various pathological processes [194].

Of the tissue preparations, the most significant interest is the use of the placenta, which is a concentrate of biologically active substances - proteins, lipids, enzymes, hormones, and many others, which leads to wide use, in particular, in the field of animal reproduction [200].

However, the problem of using preparations of plant and tissue origin has not been sufficiently studied; many aspects of their clinical use require further development, an expanded spectrum of used medicinal plants, substantiation, and introduction into veterinary practice.

Therefore, this work aimed to develop complex vitamin-hormonal preparations based on plant and tissue derivatives to treat and prevent animal reproductive pathologies.

Taking into account the direction of research and the concept of continuity and sequence, it became logical to develop effective, simple, and acceptable methods for the practice of veterinary medicine for the treatment and prevention of disorders of reproductive function in animals. It was mandatory to consider the provisions of the mechanisms of the emergence and development of pathologies and disorders of the reproductive function clarified by the article's authors. Based on the received information about the etiopathogenesis of reproductive function disorders: changes in homeostasis indicators, a decrease in the concentration of hormones (estrogens or progesterone), changes in the morpho-functional state of endocrine (pituitary, thyroid, and adrenal glands) and sexual (ovaries) organs, the use of vitamin-hormonal drugs Medicines in terms of pathogenetic therapy make it possible to normalize indicators of

homeostasis, hormone concentration, stimulate rehabilitation processes in the regulatory organs of reproductive function (pituitary, thyroid, and adrenal glands) and sexual organs (ovaries), which in turn contributes to the normalization of folliculogenesis and steroidogenesis, which is a necessary condition for the full manifestation of reproductive ability in females.

For this purpose, vitamin-hormonal preparations of plant and tissue origin "Cagadin," "Caplaestrol," "Caplagonin," and "Carafest" were developed based on a solution of β -carotene in oil, which helps to rehabilitate the structure and functional state of the genitals and reproductive organs. Functions. The drug "Cagadin" is intended for the prevention and treatment of hypovitaminosis and the fight against infertility in animals and allows:

- normalize the condition of embryos and fetuses;
- prevent hidden abortions (embryonic mortality), reduce embryonic losses in the antenatal period;
- increase the number of full-term newborns with high development potential;
- to activate the family activity;
- to prevent pathological births (hypofunction of births, dystocia, litter retention);
- to increase the rate of fertilization and the number of received newborns from the female.

The drug "Caplaestrol" is a solution of carotenoids and total estrogens. Estrogens optimize the development of fetuses, normalize the course of pregnancy and activate labor, and also contribute to the secretion of follicle-stimulating hormone in the pituitary gland, which stimulates folliculogenesis in the ovaries.

"Caplaestrol" is intended to fight against infertility and prevent obstetric and gynecological pathology. In particular, the scope of application of the drug is:

- normalization of embryo and fetus development;
- prevention of antenatal pathology;
- prevention of pathological births (hypofunction, delayed litter);
- therapy of females with postpartum gonado- and metropathies;
- increasing the vitality of newborns and their development potential.

The drug "Caplagonin" is a solution of β -carotene and chorionic gonadotropin. Due to the content of chorionic gonadotropin in the composition of the drug, it is used to increase the fecundity of females (normalization of ovulation, formation, and development of the corpus luteum) and intended to increase the fecundity of females and the reproductive capacity of males.

The drug "Carafest" is an oil solution of carotenoids and phytoestrogens and an analog of the drug "Kaplaestrol"; however, unlike the latter, it contains plant estrogens that contain a phenolic ring, which makes them similar to the spatial structure of the hormone β -estradiol and gives the ability to connect with estradiol receptors, showing a hormone-like effect.

The drug is intended to combat infertility and prevent losses during animal reproduction.

The drug "Carafand" is an oil solution of carotenoids and phytoandrogens and is intended for the treatment and prevention of a decrease in the reproductive capacity of males.

Using the developed drugs, their high therapeutic effect has been established. Thus, the implementation of a program of complex therapy of cows, sheep, and goats with gonadopathy using the drugs "Carafest," "Caplaestrol," and "Caplagonin" provides a reduction in the manifestation of signs of estrus from the start of treatment and an increase in fertility.

A comprehensive program for the prevention of perinatal pathologies using the drug "Caplaestrol" and "Carafest" allows to increase in the number of lambs and kids with satisfactory clinical conditions with high development potential, reduce their morbidity and mortality, and reduction in the number of animals with intra- and postnatal pathology in sheep and goats.

A complex program of male therapy for reduced reproductive capacity using the drug "Carafand" had a positive effect on the manifestation of sexual reflexes and sperm quality, in particular, due to the stimulation of Leydig cells with androgen-like substances in bulls, boars, and dogs, androgenesis was activated, the volume of ejaculate increased; mobility increased sperm count and sperm concentration, the

percentage of motile sperm in the ejaculate increased, the number of sperm with morphological abnormalities decreased.

Thus, the developed vitamin-hormonal preparations on a plant and tissue basis have high efficiency in the treatment and prevention of reproductive pathologies of animals of various species, providing stimulation of reproductive function during the therapy of females with gonadopathy, increasing the viability of newborns, preventing the incidence of intra- and postnatal and andrological pathology [201].

Modern requirements for theoretical and practical veterinary medicine require comprehensive implementation of adequate means and methods of treatment of animals of various species. This also applies to the use of antibacterial drugs. Hopes that antibiotics can completely solve the problem of pathologies of an infectious nature are not justified. In response to the synthesis and use of new antibacterial drugs, other strains of microorganisms appear, and viruses and fungi increasingly show their pathogenic properties.

Antibiotics are becoming increasingly complicated and expensive, and their uncontrolled use affects a highly urgent problem – obtaining high-quality food products of animal origin that are not harmful to human health.

Therefore, it is evident that it is necessary to choose such means of animal treatment, which, along with pronounced antibacterial and other therapeutic properties, would not show the mentioned negative manifestations. Such means include the treatment of animals using ozone-containing drugs, which form the basis of ozone and propolytherapy – highly effective, ecological, and economically beneficial methods of treatment that have a positive effect on the animal body without side effects.

Ozone is a highly active chemical element known as a protector of living organisms against the effects of ultraviolet rays. It is a gas with a sharp smell but feels like a pleasant freshness at deficient concentrations. In connection with the growth of human and animal allergies, the decrease in antibiotic sensitivity, and the increase in the price of medicines, non-medicinal methods are becoming increasingly popular. Therefore, along with efficiency, such a criterion as safety is put forward. In this regard, ozone therapy is promising [202].

The method has been introduced in veterinary medicine and has significant prospects in animal reproduction. The therapeutic effect of ozone is based on the known mechanisms of its biological action:

- bactericidal, fungicidal, and viricidal against the essential types of gram-positive and gram-negative bacteria, viruses, pathogenic fungi, and protozoa;
- activation of oxygen-dependent processes;
- strengthening of exchange processes of production of energy substrates;
- immunomodulating effect;
- improvement of microhemocirculation and gas exchange at the tissue level.

Propolis is a resinous substance collected by bees to seal cracks, disinfect and create a healthy environment in the hive. The effect of propolis on the body, organs, tissues, and cells is wide and varied.

1. It has pronounced bactericidal, virucidal, and fungicidal effects.
2. Activates phagocytosis and the production of specific and non-specific antibodies.
3. Increases the tone of capillaries, participates in many redox processes, has an antioxidant effect, and reduces the adverse effects of free radical oxides on the cell membrane.
4. Creates a barrier membrane (line of demarcation) on the paths of propagation and penetration of microorganisms from places of contamination and foci of inflammation into healthy, undamaged tissues.
5. It has anti-inflammatory properties.
6. It has a hemostatic effect.
7. Stimulates tissue regeneration.
8. Regulates protein, fat, and carbohydrate metabolism.
9. It positively affects the thyroid gland, adrenal glands, and gonads.
10. It has pronounced choleretic and diuretic effects.
11. It has anesthetic properties.
12. It has a pronounced deodorizing effect [191].

The developed preparations "OKO" (ozonated corn oil) and "Prozon" (a complex preparation based on ozonated corn oil and an alcoholic solution of propolis), which form the basis of ozone and propolytherapy of animals in the case of reproductive pathologies and are a joint development of the Department of Veterinary Surgery and Reproduction of the State of the University of Biotechnology (Kharkiv) and the Department of Low-Temperature Equilibrium Plasma Chemistry of the National Scientific Center "Kharkiv Physical and Technical Institute" (Kharkiv).

In the programs for the treatment of animals with reproductive pathologies (metritis, mastitis, vestibulovaginitis), the program item antibiotic, nitrofurantoin, and sulfonamide therapy has been replaced by the use of ozone-containing preparations "OKO" and "Prozon." The implementation of these programs reduces the duration of the treatment period and clinical recovery, confirmed by a decrease in the number of epitheliocytes and leukocytes and cells with a yellow-red color, which confirms the effectiveness of ozone-containing drugs and their antibacterial properties. Thus, "OKO" and "Prozon" drugs, which form the basis of ozone and propolytherapy for reproductive pathologies, provide high efficiency and economic benefits of treatment methods with a positive effect on the animal body.

The use of ozone-containing preparations for the sanitation of the preputial cavity of males and the treatment of non-specific balanoposthitis allows for improving the indicators of the post-cytogram under light-optical and luminescent microscopy qualitatively – to reduce the number of epitheliocytes, leukocytes, microbes and cells with a yellow-red color; increase the number of cells with green color; to optimize the ratio of the number of epitheliocytes and leukocytes, epitheliocytes with typical structure and dystrophy, cells with yellow-red and green color.

Today, nanotechnology demonstrates extraordinary progress, resulting from the development and merger of several scientific areas, and is one of the critical areas of industrial development and societal progress. Scientists predict this progress could be a significant breakthrough in solving some problems facing humans and veterinary medicine. Examples of potential applications in veterinary medicine include disease diagnosis and treatment systems, new tools for molecular and cell breeding, and more.

Along with traditional chemical medicines for animals, biologically active therapy is increasingly widely used, which complements chemical treatment and is aimed at using the body's self-regulation capabilities and drugs of natural origin [203].

Since nanotechnology is at a very early stage of development, it may take several years to conduct the necessary research and clinical trials to produce meaningful results. This tool, developed over the next several decades, will have significant implications in veterinary and animal science [204].

Thanks to bionanotechnologies, new methods of introduction and delivery of vaccines and drugs have appeared by fixing them on nanoparticles (nanocapsules, nanotubes, nanospheres, fullerenes, dendrimers, liposomes), ligands of directed action, "point" delivery to competent organs and cells, dose reduction and ensuring the prolonged effect of drugs. The use of nanotechnologies as antimicrobial, antifungal, antiprotozoal, and antiviral chemotherapy in surgery and traumatology, homeopathy, and vaccine prophylaxis is known.

In veterinary medicine, nanotechnologies are used to solve several tasks, the main of which are:

- development of highly effective and express methods of diagnosis of infectious and invasive diseases of animals;
- indication and identification of pathogens;
- the creation of means of protection (vaccines) with high immunogenicity and low reactogenicity;
- development and application of DNA technologies in animal breeding;
- design of new medicines and their delivery to targets in the body of a sick animal;
- the creation of means that increase the resistance of animals - probiotics, interferons, interleukins, immunomodulators, etc.);
- production of biologically active substances (amino acids, antibiotics, enzymes, vitamins, hormones, etc.) to stimulate the growth and increase the productivity of animals;

- an increase of feed resources through the production of feed protein, protein-vitamin concentrates, and essential amino acids using agricultural production waste;
- the creation of biological means of protecting animals and plants;
- replenishment of feed protein deficit of food resources with new sources;
- improvement of environmental protection with the use of microorganisms;
- solving energy problems by converting plant biomass and livestock waste into biogas and biofuel;
- Environmental Protection.

Nanoparticle technologies could change the landscape of the pharmaceutical industry and revolutionize the drug development process in the coming decades. Due to their unique physical and chemical properties, nanoparticles are promising for the targeted delivery of a wide range of molecules to the required body tissues. Nanoparticle technologies can increase the therapeutic index of drugs by increasing their effectiveness and/or improving their tolerability by the body. Nanoparticles can also increase the bioavailability of water-insoluble drugs, protect active substances from physiological factors, and enable the development of new classes of biologically active macromolecules (for example, DNA).

In recent decades, considerable attention has been paid to the study of metal nanoparticles, which indicates their use in technologies for constructing highly effective means of diagnosis and targeted therapy. Yes, colloidal gold has been known since ancient times and was used for medicinal purposes. There are data on a significant enhancement of the properties of antibiotics and anticancer agents due to their conjugation with nanogold and the positive effect of gold nanoparticles on the functional activity of macrophages.

Examples of nanobiomaterials are also known in the field of animal reproduction. For example, promising biocidal nano preparation has been developed that protects pathogenic microflora without disrupting the genome of heredity by purposefully regulating the processes of nutrient metabolism and increasing animal productivity by increasing the digestibility of plant feed [205].

The use of modern veterinary homeopathic drugs for treating and preventing animal diseases makes it possible to widely introduce nanotechnological methods of reproductive function regulation into the practice of veterinary medicine. Thus, the drugs "Liarsin" and "Mastometrin" ensure a positive and influential effect on animal reproductive capacity, help increase productivity, preserve young animals, and reduce their morbidity.

The influence of highly dispersed silicon dioxide nanoparticles on sperm apoptosis, cryoresistance of devitrified oocyte-cumulus complexes, and the development of pre-implantation *Bos taurus* embryos was studied. The percentage of necrotic cells fluctuated slightly; the percentage of intact cells decreased in proportion to the increase in the percentage of sperm with reduced mitochondrial potential. The obtained data expand the understanding of the mechanisms of influence of silicon-containing nanomaterials on the viability of male gametes and destructive processes in sperm chromatin. The study's results should be considered for further optimization of sperm cryopreservation methods.

The nature of the influence of silicon dioxide nanoparticles on the indicators of cryoresistance of somatic (cumulus), germ cells (oocytes) of ovarian follicles of cows, and egg fertilization has been identified. The positive effect of highly dispersed silica nanoparticles on the preservation and functional state of cumulus cells after devitrification and cultivation of oocyte-cumulus complexes was revealed. It was established that the introduction of nanoparticles of silicon dioxide into the culture medium of gametes provided a significant increase in the level of fertilization of oocytes and the proportion of embryos that reached the final stage of pre-implantation development – blastocysts. The obtained data contribute to a better understanding of the mechanisms of the functioning of somatic and germ cells of ovarian follicles in ultra-low temperatures and indicate the feasibility of using silicon dioxide nanoparticles to modernize the maturation system of donor oocytes of cows by introducing it into the medium for cultivation.

Promising biocidal nanopreparations have been developed that protect against pathogenic microflora without disrupting the genome of heredity by targeted regulation

of nutrient metabolism processes and increasing animal productivity by increasing the digestibility of plant feed. Nanoparticles of drugs made from embryonic-placental fluid and tissue have therapeutic immunological, genetic, and diagnostic properties. Their components - immunoreactive peptides- positively affect cellular and humoral immunity and metabolic processes and perform a restorative role in inflammatory processes. In particular, their use increases the fertility of cows.

Complex drug Sodekhin K-75, the active substances of which are glycyrrhizic and oxycinnamic acids and silver ions, is used to increase immunobiological resistance, prevent infertility and obtain healthy offspring.

Based on comprehensive research, the feasibility of using complex biological preparations PS-2 and Prevention-N-A in herd reproduction technology to prevent gynecological diseases and increase reproductive function has been scientifically substantiated and experimentally proven. Under the influence of the drug in cows, the time of separation of fetal membranes was shortened, litter retention, postpartum complications, and diseases of the mammary gland were prevented. Against the background of immune correction, the timing of the onset of sexual desire in cows decreased, the insemination index decreased, the service period was shortened, and fertilization in the first heat increased.

Sapropel prophylaxis, sapropel stimulation and sapropel therapy, and Tyumen mineral water for veterinary and gynecological practice are proposed as components of therapeutic and preventive measures for reproductive disorders and infertility in cows.

Promising directions include the use of metal nanoparticles. The action of trace elements, both in ionic and especially in nanoform, does not have a direct unidirectional effect (unlike antibiotics and hormones). This is an indisputable advantage, as the animal receives a complex benefit - improving the entire body by activating its forces, increasing adaptability, strengthening immunity, and stimulating all vital functions, including reproduction.

To intensify the reproductive function of cows in the postpartum period, a metal-polymer composition MPK-3K of nanoparticles of Cu, Fe, and Zn obtained by the

evaporation-condensation method with an average particle size of 80 nm and a specific surface area of about 8.0-10.0 square meters was used. m per gram of powder. It was established that such a metal-polymer composition has a modifying effect on physiological processes in the body of cows. This is reflected in the activation of biosynthetic and energy processes in the body and stimulation of the cellular link of immunity.

The use of nanoaquachelates of metal colloids for treating cows suffering from mastitis and stimulating the reproductive function of cows, bulls, pigs, sheep, and goats is proposed.

In pregnant rabbits and sows, under the influence of chromium citrate, various links of metabolism are corrected; in particular, the glucose content in the blood stabilizes, the amount of glycogen in the liver and skeletal muscles increases, the hexokinase and lactate dehydrogenase activity of erythrocytes increases, the content of total protein increases, and the content of triacylglycerols and cholesterol decreases in the blood of animals, the antioxidant system and indicators of lipid peroxidation are normalized, as well as the state of the body's immune defense is improved. Metabolically adequate amounts of chromium citrate, which were additionally introduced into the diets of rabbits and pigs, can be used as recommended doses for regulating metabolic processes and preventing Chromium(III) insufficiency in the body.

Nanoaquachelates of such metals as Argentum, Cuprum, and Ferum significantly strengthen the specific and non-specific resistance of the animal organism. Nanoparticles of these metals have biocidal properties and are also powerful microelement nanoaquachelates, which are much more effective than microelements in the classic ionized form. The combination of the effect of nanodisinfectants with the animal organism's own microbial, viral, and fungicidal activity, as well as with the stimulating effect of increasing the resistance of animals, can create the necessary conditions for providing animals with highly effective preventive and curative care.

In veterinary medicine, drugs developed based on nanoparticles are successfully used to diagnose, treat, and prevent diseases of various etiologies. Providing macro-

and microelements to animals in the form of nanoparticles has several advantages: nanoaqua-chelates of biometals have a high biological effect; thanks to their nano size, they are more fully absorbed by the body and are actively used in metabolic processes. However, the mechanism of action of nanomaterials on the animal body is insufficiently studied and requires more in-depth research. The high efficiency of using metal nanoparticles is due to their participation as cofactors in biochemical reactions and as activators of regenerative processes in the animal body. One of the main reasons for the change in the physical and chemical properties of small particles as their size decreases is the increase in the relative number of "surface" atoms. A decrease in particle size leads to an increase in the accessible surface area of a substance, and from an energy point of view, to an increase in surface energy. Thanks to this effect, nanometals have unique properties. Metal nanopowders are compassionate catalysts, sensor systems, and humane and veterinary medicine medicines. The high economic efficiency of using Argentum, Cuprum, and Ferum nanoaqua-chelates in treating mastitis and endometritis has been proven.

Ferrum is one of the most important chemical elements that provide the basis for the vital activity of animal organisms. This element plays an essential role in the body's recovery processes, immunological reactions, blood formation processes, and the course of almost all metabolic reactions in the growth and development of the body. The use of nanolysis in the diet of animals and the introduction of sterile solutions showed that such forms of nanopowder contribute to the activation of factors of non-specific immunity (phagocytic reaction, bactericidal and lysozyme activity of blood serum) and specific activity of immunity (activates cells of the red bone marrow, thymus, spleen, lymph nodes). Cultivation of some pathogenic bacteria with the addition of nano-dispersed iron to the liquid medium reduced their virulence and pathogenic properties.

Copper is a necessary metal for the body's normal functioning, which participates in many essential metabolic processes and exhibits significant bacteriostatic and bactericidal activity due to damage to plasma membranes. The mechanism of antibacterial action of copper is based mainly on the disruption of the

DNA structure. Nanoparticles of copper, introduced into the body of animals, are characterized by prolonged activity and lower toxicity compared with copper salts. Studies of the mechanism of action on bacteria indicate a violation of the barrier properties of bacterial membranes when interacting with copper particles. Still, it cannot be claimed that the discovery of the mechanism is complete and does not require further experimentation. Studies have shown that copper nanoparticles, unlike antibiotics, do not cause the selection of resistant strains of microorganisms, which allows us to further recommend nano copper in the treatment of purulent-septic diseases caused by polyantibiotic-resistant strains of *Staphylococcus aureus*.

Silver nanoparticles are incredibly active and cause the death of bacteria, viruses, and fungi due to their large specific surface area, which increases the size of contact of silver with pathogens of infectious diseases, significantly growing its bactericidal properties. When considering the evolution of silver from ions to nanoparticles and studying the effect of various silver preparations on viruses, bacteria, and cells, it was established that the biocidal effect of silver nanoparticles significantly exaggerates the effect of silver ions in the same concentrations. Silver nanoparticles are active against microorganisms resistant to antibiotics, which makes it possible to use them for many infectious diseases. The high biological activity of microelements-metals in the body is connected, first of all, with their participation in synthesizing some enzymes, vitamins, and hormones. Depending on the concentration, silver cations can both stimulate and inhibit the activity of some enzymes. Under the influence of silver, the intensity of oxidative phosphorylation in brain mitochondria is doubled, and the content of nucleic acids increases, which improves the function of the central nervous system. An increase in the concentration of silver ions to 0.01 μg reduces the degree of oxygen absorption by the cells of these organs, indicating the participation of silver cations in regulating energy metabolism. Silver ions have antiseptic activity – silver nanoparticles, 10-30 nm in size, cause a pronounced antibacterial effect and are used for local treatment of infected skin wounds. It has been established that nanosilver solutions are the most effective means of direct contact with surfaces inflamed due to bacterial infection. Silver nanoparticles, due to their small size and other

physicochemical properties, are highly active and cause the death of various microorganisms: bacteria, viruses, and pathogenic fungi. The use of silver in the form of nanoparticles makes it possible to significantly reduce the concentration of silver while maintaining antimicrobial properties, including for microorganisms resistant to antibiotics. Other significant effects of nanosilver are anti-inflammatory and immunomodulatory. Researchers attribute these effects to the inhibition of the synthesis of cytokines, such as TNF- α , IL-12, IL-18, and matrix metalloproteinases, in particular, MMP-9.

In the prevention and treatment of obstetric pathology of cows, the problem of diseases caused by conditionally pathogenic microflora is quite acute. In this regard, antibacterial drugs are widely used to prevent and treat this pathology. However, the use of antibiotics is not always practical. It has the risk of accumulating in muscles and passing into milk, which forces veterinary medicine to look for more effective means of combating opportunistic pathogens. Considering these factors, it is advisable to study the use of nanoaquachelates of metals, which have antiseptic properties and various stimulating activities – hematogenous, immunogenic, regenerative, etc. Nanoaquachelates of metals have a complex effect in the absence of toxic and side effects, do not cause habituation of microflora, do not reduce the quality of the obtained product, and are characterized by a relatively low cost.

The nanoaquachelate form significantly enhances all antiseptic and biogenic properties of metals without exception, which gives their application a special etiotropic and pathogenetic usefulness. Obstetric pathologies cause long-term infertility of cows, their premature culling, the birth of dead and unviable fetuses, and the unprofitable use of fodder, which causes significant economic losses to farms. When comparing the therapeutic effect of nanoaquachelates of metals with ichthyofuran sticks and levotetrasulfine, the best therapeutic effect was obtained when cows were treated with a solution of nanoaquachelates of metals (recovery was higher, and the duration of treatment was shortened). It can be concluded from this that the treatment with nanoaquachelates of metals is quite effective in treating postpartum pathologies.

The possibility of preventing postpartum complications with drugs containing nanoaquachelates of metals deserves attention. The prophylactic effectiveness of drugs with nanomaterials was compared to furazolidone sticks in cases of normal calving and after surgical interventions. When using nanoaquachelates of metals in cows, the duration of subinvolution of the uterus and the period from calving to the manifestation of estrus were shortened, and fertility increased.

Using a class of complex compounds of nanoaquachelates in medical practice is an alternative to using antibiotics in the therapy of productive animals, which prevents the risk of antibiotic-induced pathologies in consumers of animal products. Unlike antibiotics and fluoroquinolones, causative agents of bovine mastitis are sensitive to the complex of metal nanoaquachelates. When treating cows with mastitis with metal nanoaquachelates, the number of cases of inflammation transitioning into a hidden form was reduced, the occurrence of mastitis was prevented, the incidence of endometritis was reduced when the litter was retained, the duration of uterine involution and the service period was shortened.

The positive effect of suppositories containing copper nanoparticles on the activation of the humoral link of the body's immune system and the creation of prerequisites for the restoration of reproductive function after childbirth (increase in the content of class A and G immunoglobulins and decrease in the content of class M immunoglobulins, shorten the duration of the service period, reduce the insemination index) has been established.

An antibacterial drug based on nanotechnology, "Iodprotectin," has been developed with therapeutic efficacy for endometritis and mastitis of various forms.

Employees of the Department of Veterinary Surgery and Reproduction of the State University of Biotechnology (Kharkiv) and the Department of Nanocrystalline Materials of the Institute of Scintillation Materials of the National Academy of Sciences of Ukraine (Kharkiv) improved several vitamin-hormonal preparations used in the schemes of therapeutic and preventive measures for obstetric, gynecological, andrological and mammological pathologies of animals. In particular, in order to increase the therapeutic effects of drugs containing carotenoids, estrogens, and

androgens, the addition of substances that affect the pro-oxidant-antioxidant system and oxygen metabolism – nanoparticles of cerium dioxide (DC) and orthovanadate (OV) of rare earth elements, which can also penetrate cells and accumulate in the nuclei.

The use of these drugs makes it possible to optimize individual indicators of homeostasis and the pro-oxidant-antioxidant system (the content of carotene, vitamin A, zinc, total protein, albumins, total globulins and fractions α_1 , α_2 , β and γ , malondialdehyde, catalase, superoxide dismutase, in erythrocytes of malondialdehyde, catalase, and reduced glutathione, as well as indicators of the pro-oxidant-antioxidant ratio and oxygen metabolism - the number of erythrocytes, the hemoglobin content and the concentration of 2,3-diphosphoglycerate).

Thus, the drugs "Caplaestrol+DC," "Caplaestrol+OV," "Cagadin+OV," "Carafest+OV," and "Carafand+OV" allow to normalize the structure and function of the fetoplacental complex of cows, sows, rabbits, sheep, and goats and increase the development potential of newborn calves, piglets, rabbits, lambs and goats [194].

In addition, the drug "Caplaestrol+OV" proved to be effective in the treatment of cows with mastodystrophy during the dry and lactation periods, ensuring the normalization of the cytogram of the mammary gland secretion, thermo-, and sonogram types, as well as reducing the number of microbes and somatic cells (leukocytes and epitheliocytes).

Using the drugs "Caplaestrol+OV" and "Caplaestrol+DC" made it possible to increase the effectiveness of the therapy of cows and goats for gonadopathy. Thus, the use of the drugs "Caplaestrol+OV" for gonadodystrophy and "Caplaestrol+DC" for hypogonadism ensured a reduction in the periods from the beginning of treatments to the repair of the ovaries and the manifestation of estrus, as well as an increase in fertility and a reduction in the duration of infertility days.

With diorgan pathology (hypoluteolysis ↔ subclinical metritis), the drug "Caplaestrol+OV" made it possible to shorten the clinical recovery of cows and goats and the period after treatment until the manifestation of estrus with an increase in fertility after the first insemination.

The drug "Carafand+OV" helps to improve the indicators of the content of carotene, vitamin A and zinc in the blood serum, normalize the balance of the pro-oxidant-antioxidant system, normalize the dynamics of oxygen metabolism, increase the level of testosterone in the blood serum, restore sexual reflexes, normalize post-, thermo- and sonograms and overall positive effect on sperm characteristics - increase in ejaculate volume, increase in sperm concentration and mobility, decrease in the content of sperm with morphological abnormalities in boars and bulls.

Along with this, the widespread use of nanomaterials has raised concerns about the potential toxicity of nanoparticles. Different types of nanoparticles adversely affect male germ cells, the female reproductive system, and fetal development, especially given the small size of nanoparticles, their ease of penetration and biocompatibility, and potential ability to disrupt the placental barrier. These effects are related to nanoparticle modification, composition, concentration, route of administration, and animal species.

Due to daily exposure, early studies show that nanoparticles accumulate and bind to body cells, disrupting normal physiological systems. In addition, nanoparticles are associated with various disorders, including lung injury, hepato-, neuro-, immuno-, renal toxicity, and irreversible testicular damage.

However, in other studies, such an effect is disputed or not confirmed, depending on several conditions, such as, for example, the nature, type, and size of the nanoparticles, as well as the dose and possibly the route of administration. Furthermore, nanoaquachelates of metals have a complex effect in the absence of toxic and side effects, do not cause habituation of the microflora, do not reduce the quality of the obtained product, and are characterized by a relatively low cost.

In addition, the problem is also related to the fact that the studies were not conducted consistently and, therefore, are difficult to compare. To fill this gap, closer collaboration between nanotoxicologists and reproductive scientists is needed to develop and interpret results, as well as specific hypotheses and understandings of certain aspects of research.

The development of reproduction technologies in animal husbandry is related to biotechnology - an interdisciplinary field that arose at the junction of biological, chemical, and technical sciences:

- biophysics, the use of which allows obtaining materials about the molecular structure and functions of the membrane apparatus of cells, the mechanisms of membrane permeability and metabolism;

- cryobiology, which makes it possible to develop the theory of cryodamage and cryoprotection of cells, which is necessary for the creation of production technologies for long-term storage of genetic material - sperm, eggs, embryos and their fragments;

- electroradiophysiology, which allows searching for ways to control the body's mechanisms by transmitting the necessary information with the help of a modulated microwave field directly to the centers of the endocrine and hormonal systems;

- cytoengineering and microsurgery - for carrying out engineering works at the cellular level to create new genomes, their cloning, and reproduction;

- non-infectious immunology, which makes it possible to apply methods of radioimmunoassay and immunoenzymatic analysis of the physiological state of the body;

- hybridoma and clonal immunology, which provides the possibility of creating industrial technologies for the production of particular immune reagents and biologically active compounds;

- reproductive endocrinology – for studying and managing humoral regulation systems of reproductive processes;

- cryoengineering – for the creation of new designs of cryogenic equipment and the introduction into practice of new biotechnologies of reproduction;

- several other sciences that were not previously used in biology, especially animal husbandry.

Thanks to this, today, in addition to the most well-known methods of animal reproduction biotechnology, embryo transplantation and artificial insemination of animals, xenotransplantation, parthenogenesis, cloning, obtaining chimeras, breeding

transgenic animals, in vitro fertilization of oocytes, dividing sperm by sex, dividing the embryo into parts (single-egg twins), cryopreservation of sperm and embryos [206].

The use of methods of reproductive biotechnology made it possible to achieve significant achievements in animal husbandry and remains a prospect that will make it possible to significantly accelerate the reproduction of valuable and creation of new genotypes, intensify the selection process and increase the genetic potential of agricultural productivity of animals. Thus, methods of stimulation and synchronization of the sexual cycle have been developed by biological science, which contributes to the improvement of the functional state of the reproductive apparatus, restorative and corrective processes of sexual function, elimination and prevention of the causes of functional deviations, reduction of the duration of infertility, and, accordingly, increase of animal productivity [207].

Conclusions

1. Modern programs for diagnosing reproductive pathologies, predicting the course of childbirth, assessing the condition of embryos/fetuses, and the clinical condition of newborns are based on the developments of related sciences and allow to reveal objective information, justify and implement appropriate therapeutic or preventive measures promptly.

2. The use of nanoparticles with a studied effect on the composition of drugs provides an opportunity for a more comprehensive introduction of nanotechnological methods into the practice of reproductive veterinary medicine with predictable consequences and high efficiency.

3. Innovations in veterinary reproductive science include the latest developments and achievements of related biological, chemical, technical, and physical sciences.