



UDC 636.3:619:618.1

DOI: 10.48077/scihor.24(8).2021.15-25

## The Development of Phyto- and Tissue Origin Medicines for Veterinary Reproductive Issues

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### Article's History:

Received: 15.08.2021

Revised: 16.09.2021

Accepted: 18.10.2021

### Suggested Citation:

Skliarov, P., Fedorenko, S., Naumenko, S., Koshevoy, V., & Pelyh, K. (2021). The development of phyto- and tissue origin medicines for veterinary reproductive issues. *Scientific Horizons*, 24(8), 15-25.

**Abstract.** Modern conditions of practical veterinary medicine require the use of effective and safe drugs. Along with the already known and common medicines, the search for new drugs which are harmless for the body and have the physiological direction of action is still required. In recent years, the attention to the use of phyto- and tissue-derived drugs increased. However, the problem of their use is insufficiently studied – many aspects of their clinical use require further development, expansion of the spectrum of used medicinal plants, study, and implementation into veterinary practice. Therefore, the purpose of this work was to develop a comprehensive vitamin-hormone drugs based on phyto- and tissue medicines for the treatment and prevention of reproductive abnormalities in animals. Based on the information on the etiopathogenesis of disorders of reproductive function indicators: homeostasis, reducing of the concentration of hormones (estrogen or progesterone), changes in the morphofunctional state of endocrine (pituitary, thyroid, and adrenal gland) and reproductive (ovaries) organs, the application of vitamin-hormone drugs in veterinary medicine is scientifically sound. Drugs in terms of pathogenetic therapy can optimise homeostasis, hormone concentrations, stimulate rehabilitation processes in the regulatory organs of reproductive function (pituitary, adrenal, and thyroid) and reproductive organs (ovaries), which, in turn, contributes to the normalisation of follicles which are a prerequisite for the full reproductive capacity of females. Vitamin-hormonal medicines of herbal and tissue origin were developed, with high efficiency for the treatment and prevention of reproductive pathologies of various species of animals, providing the stimulation of reproductive function (estrus signs) for therapy of females with gonadopathies (“Carafest”, “Caplaestrol” and “Caplagonin”) and males (display of sexual reflexes and sperm quality) for reproductive activity dysfunction (“Carafand”), increase in the viability of the newborn (increasing the number of lambs and goatlings with satisfactory clinical condition with a high-growth potential, reduce in their morbidity and lethality), preventing the incidence of intra- and postnatal (labor hypofunction, diseases of post-labor period) pathology (“Carafest”, and “Caplaestrol”)

**Keywords:** animals, males, females, newborns, reproductive pathologies, treatment, prevention



## INTRODUCTION

Modern conditions of practical veterinary medicine require the use of effective and safe drugs [1-6]. Application of biotechnological methods in reproductive managing has to serve the maximum use of the reproductive potential of the animals, providing in-depth knowledge of and adherence to the biological patterns of reproduction and use of these methods in animals with optimal health and physical condition [7-11]. In particular, such an important technological milestone of the animal industry as reproduction involves the use of hormonal drugs [12-18]. However, using one or another hormonal drug, it should be kept in mind that the action on the female reproductive system can be shown in different ways – depending on the source of the functional state of the reproductive organs and the hormonal status of the body. The wrong use of the drug, regardless of criteria, can have negative effects [19-22]. Although not all scientists share this perspective and didn't find the negative impact even of multiple uses of hormonal drugs on sexual function, that should be associated with the optimisation of the dose of used drugs [23-28].

Along with the already known and common medicines, the search for new drugs, which are harmless for the body and have the physiological direction of action, is still required. In recent years, attention to the use of both human and veterinary phytomedicines increased [29-33]. Many plants contain biologically active substances, among which special attention should be paid to a plant hormone that is relevant and logical for the practice of reproductive veterinary medicine. The range of action of these substances is vast (phytoestrogens, antiestrogens, antigonadotropins), which allows using them to treat animals with different pathological processes [34-37].

Among tissue derivatives, the use of the placenta is of the greatest interest since it is a concentrate of biologically active substances – proteins, lipids, enzymes, hormones, and many others that encourage its wide use, in particular, in the field of reproduction of animals [38-43].

However, the problem of the use of phyto- and tissue-derived drugs is insufficiently studied, many aspects of their clinical use require further research, expansion of the spectrum of used medicinal plants, study, and implementation into veterinary practice.

Therefore, *the purpose of this work* was to develop a comprehensive vitamin-hormone drugs based on phyto- and tissue medicines for the treatment and prevention of reproductive abnormalities in animals.

## MATERIALS AND METHODS

The research was conducted at the Department of veterinary reproductive medicine and practical complex of the animal industry and crop science of Kharkiv State Zooveterinary Academy, control of medicines was conducted in the State Institution "V. Danilevsky Institute for Endocrine Pathology Problems of the NAMS of Ukraine" (Kharkiv) and in State Scientific-Research Control Institute

of Veterinary Medicinal Products and Feed Additives (Lviv), experimental verification and approbation took place in farms of different forms of ownership of the eastern, central and the southern regions of Ukraine.

$\beta$ -carotene was obtained from crops that contain a significant amount of this substance (grass meadow, green mass of alfalfa, carrot, pumpkin) by extraction.

Total estrogens and chorionic gonadotropin were obtained from the female placenta by extraction.

Phytoestrogens and phytoandrogens were obtained from plants such as oregano (*Origanum Vulgare*), red clover, hop, millet (bran), acorus (*Acorus calamus*) [44].

The content of  $\beta$ -carotene in preparations was titrated for calorimetry scale, and estrogen – using Kober's reaction (standard – ampule solution of synoestrol).

Prepared drugs were packed in bottles or vials of dark glass with 10, 20, 50, 100 cm<sup>3</sup> of volume, sealed with rubber or aluminum caps or plastic stoppers or lids, and were autoclaved. They were kept in a dry, protected from light place at a temperature of 5°... 15°C for up to 1 year.

The effectiveness of the program of complex therapy of females for gonadopathy was determined among 339 cows, 77 sheep, and 35 goats.

According to the comprehensive program for the prevention of perinatal pathologies, 393 sheep and 104 goats were treated, as well as 512 lambs and 125 goats were evaluated.

A comprehensive program of therapy for males with reduced reproductive capacity was applied to 17 bulls, 29 boars, and 15 dogs.

Assessing the state of the structure and function of the testes, the manifestations of conditioned and unconditioned reflexes, sperm quality, and its fertilising ability, a conclusion concerning the reproductive capacity of males is made.

## RESULTS

Regarding the direction of the research and the concept of continuity and consistency, it was logical to develop an effective, simple, and susceptible to practice veterinary medicine methods of therapy and the prevention of disorders of reproductive function in animals. The mechanisms of origin and development of pathologies and disorders of the reproductive function were obligatory to be encountered. Based on the information of etiopathogenesis of disorders of reproductive function indicators: homeostasis, reducing of the concentration of hormones (estrogen or progesterone), changes in the morphofunctional state of endocrine (pituitary, thyroid, and adrenal gland) and reproductive (ovaries) organs, the application of vitamin-hormone drugs should become scientifically effective. Preparations in terms of pathogenetic therapy can normalise the indices of homeostasis, the concentration of hormones stimulates the rehabilitation processes in organs-regulators of reproductive

function (pituitary, adrenal, and thyroid) and reproductive organs (ovaries), which, in turn, contributes to the normalisation of follicle- and steroidogenesis, which are prerequisite for total reproductive capability in females.

For this purpose, vitamin-hormone preparations of phyto- and tissue origin "Cagadin", "Caplaestrol", "Caplagonin" and "Carafest" were developed. The basis of all drugs is "Cagadin", which is a solution of  $\beta$ -carotene in oil (Table 1 and 2).

**Table 1.** The composition of "Cagadin" (1.0 ml)

Carotene, mg	10.0±0.75
Refined oil, ml	Up to 1.0

$\beta$ -carotene contributes to the rehabilitation of the structure and the functional state of the reproductive organs and the regulation of reproductive function, so the preparation "Cagadin" is intended for the prevention and treatment of vitamin deficiency and infertility. In particular, this preparation allows:

- to normalise the status of embryos and fetuses;
- to prevent hidden abortion (embryonal deaths), reduce the loss of embryos in the antenatal period;

- to increase the health of the newborns with high potential of growth;
- to increase the birth activity;
- to prevent pathological families (hypofunction of birth activity, dystocia, litter delay);
- to increase the number of fertilised females and the number of newborns from each female.

The preparation "Caplaestrol" is a solution of carotenoids and total estrogen (Table 3 and 4).

**Table 2.** Organoleptic indexes of "Cagadin"

Index	Characteristic and norm
Appearance	Transparent oily liquid
Color	From dark-yellow to brown
Smell	No specific smell
Identity	Corresponds

**Table 3.** The composition of "Caplaestrol" (1.0 ml)

Total estrogens according to RD, mg	1.00±0.05
Carotene according to RD, mg	10.0±0.75
Refined oil according to SSU 4492, cm <sup>3</sup>	Up to 1.0

Estrogens optimise the development of the fetus, normalise the course of pregnancy and activate the birth activity, as well as promote the secretion of

follicle-stimulating hormone in the pituitary gland that stimulates folliculogenesis in the ovaries.

**Table 4.** Organoleptic indexes of "Caplaestrol"

Index	Characteristic and norm
Appearance	Transparent oily liquid
Color	From dark-yellow to brown
Smell	Specific
Mass fraction of carotenoids, mg/cm <sup>3</sup>	10.0±0.75
Mass fraction of total estrogens, mg/cm <sup>3</sup>	1.0±0.05

"Caplaestrol" is intended for infertility treatment, prevention of obstetric-gynecologic pathology. In particular, the scope of use of this preparation is:

- normalisation of the development of an embryo and a fetus;
- prevention of antenatal pathology;
- prevention of pathological birth (hypofunction,

litter delay);

- therapy of females with post-natal gonado- and metropathies;
- improving the viability of newborns, potential of their development.

The preparation "Caplagonin" is a solution of  $\beta$ -carotene and chorionic gonadotrophin (Table 5 and 6).

**Table 5.** The composition of "Caplagonin" (1.0 ml)

Chorionic gonadotrophin, mg	15±0.5 mg
Carotene, mg	10.0±0.75
Refined oil, ml	Up to 1.0

Due to the contents of the chorionic gonadotrophin in the composition of the preparation, it is used to enhance the reproductive health of females (normalise ovulation as well as formation and development of yellow body).

**Table 6.** Organoleptic indexes of "Caplagonin"

Index	Characteristic and norm
Appearance	Transparent oily liquid
Color	From dark-yellow to brown
Smell	No specific smell
Identity	Corresponds

Designed to enhance the fertility of females and the reproductive ability of the males. The preparation "Carafest" is an oil solution of carotenoids and phytoestrogens (Table 7 and 8).

**Table 7.** The composition of "Carafest" (1.0 ml)

Phytoestrogens according to RD, mg	1.0±0.05
Carotenoids according to RD, mg	10.0±0.75
Refined oil according to NSSU 4492, cm <sup>3</sup>	Up to 1.0

"Carafest" is similar to "Caplaestrol", however, unlike the latter, it includes plant estrogens. They include phenol ring, which makes them similar to the spatial structure of the hormone  $\beta$ -estradiol, which allows them to bind to receptors of estradiol, exhibiting hormone-like activity.

**Table 8.** Organoleptic indexes of "Carafest"

Index	Characteristic and norm
Appearance	Transparent oily liquid
Color	From dark-yellow to brown
Smell	Specific
Mass fraction of carotenoids, mg/cm <sup>3</sup>	10.0±0.75
Mass fraction of phytoestrogens, mg/cm <sup>3</sup>	1.0±0.05

Designed for infertility treatment and to prevent losses in animal reproduction. "Carafand" is an oil solution of carotenoids and phytoandrogens (Table 9 and 10).

**Table 9.** The composition of "Carafand" (1.0 ml)

Phytoandrogens according to RD, mg	1.0±0.05
Carotenoids according to RD, mg	10.0±0.75
Refined oil according to NSSU 4492, cm <sup>3</sup>	Up to 1.0

**Table 10.** Organoleptic indexes of "Carafand"

Index	Characteristic and norm
Appearance	Transparent oily liquid
Color	From dark-yellow to brown
Smell	Specific
Mass fraction of carotenoids, mg/cm <sup>3</sup>	10.0±0.75
Mass fraction of phytoandrogens, mg/cm <sup>3</sup>	1.0±0.05

It is intended for the treatment and prevention of fertility reduction in males. When applying the preparations, it is necessary to balance animal rations for protein, calcium, phosphorus, magnesium, and microelements.

The application of preparations developed by the authors shows high therapeutic effect, as evidenced by the obtained data (Table 11).

**Table 11.** The results of the preparation use in schemes for prevention and treatment of reproductive pathologies

Actions (therapeutic or prophylactic)/Reproductive pathology	Drug	Therapeutic effect
The complex therapy program of females with gonadopathies	"Capla-estrol"	Symptoms of estrus from the beginning of the treatment – 30.5±0.4 days for 85% of fertilisation (cows)
	"Cara-fest"	Symptoms of estrus from the beginning of the treatment – 40.5±1.05 days for 75% of fertilisation (cows)
	"Capla-estrol" + "Capla-gonin"	Symptoms of estrus from the beginning of the treatment: – sheep – 62.5%-76.9% for 60.0%-80.0% of fertilisation; – goat – 57.1%-66.7% for 70%-75% of fertilisation
The complex program of prevention of perinatal pathologies	"Capla-estrol"	<ol style="list-style-type: none"> <li>1. Clinical status and the potential of development: – reducing the number of lambs in unsatisfactory clinical condition with low potential of development by 11.1% and young kids by 5.4%; – increase the number of lambs in satisfactory clinical condition with high potential of development by 10.6% and of young kids by 8.6%.</li> <li>2. Reducing morbidity: – lambs – by 9.5%; – young kids – by 7.4%.</li> <li>3. Reducing lethality: – lambs – by 7.5%; – young kids – by 4.2%.</li> <li>4. Prevention of intranatal pathology (genera hypofunction) – sheep – by 13.5%; – goat – by 14.4%.</li> <li>5. Prevention of postnatal pathology: – lambs – by 8.2%; – goat – by 8.7%</li> </ol>
	"Cara-fest"	<ol style="list-style-type: none"> <li>1. Clinical status and the potential of development: – reducing the number of lambs of unsatisfactory clinical condition with low potential of development by 12.9% and young kids by 5.9%; – increase the number of lambs with satisfactory clinical condition with high potential of development by 12.2 and young kids by 8.8%.</li> <li>2. Reducing morbidity: – lambs – by 11.1%; – young kids – by 7.9%.</li> <li>3. Reducing lethality: – lambs – by 8.2%; – young kids – by 5.9%.</li> <li>4. Prevention of genera hypofunction: – sheep – by 14.8%; – goat – by 16.1%.</li> <li>5. Prevention of postnatal pathology: – lambs – by 8.8%; – goat – by 9.7%</li> </ol>
The complex therapy program of males with reduced fertile ability	"Cara-fand"	<ol style="list-style-type: none"> <li>1. Improving the quality of semen: – bitterns: increase the volume of the ejaculate – by 28.2%, mobility of spermatozoa – by 6%, concentration – by 17.1%, moving spermatozoa in the ejaculate – by 56.8%, spermatozoa percentage of morphological anomalies decreased in 2.2 times; – boars: the volume of the ejaculate by 23.1%, mobility – by 16.4%, concentration – by 4.4%, amount of moving spermatozoa in the ejaculate – by 61.3%; spermatozoa percentage of morphological anomalies decreased in 1.2 times; – canines: the volume of the ejaculate increased by 36.1%, mobility – by 22.8%, concentration – by 45.1%, amount of moving spermatozoa in the ejaculate – in 2.1 times, pathological forms of spermatozoa decreased in 1.7 times.</li> <li>2. Activation of androgenesis: – boars – in 5.5 times; – canines – in 4.9 times</li> </ol>

As can be seen, the implementation of a complex therapy program of cows with gonadopathies using "Carafest" provides the display of symptoms of estrus in 30.5 days with 75% of fertilisation and in 40.5 days and 85% of fertilisation using "Caplaestrol" respectively. The scheme of treatment of gonadopathies using "Caplaestrol" and "Caplagonin" provides the display of symptoms of estrus from the beginning of treatment in 62.5-76.9% of the sheep and 57.1-66.7% of goats by fertilisation of 60.0-80.0% and 70-75% respectively.

A complex program of prevention of perinatal pathologies with the use of "Caplaestrol" allows increasing the number of lambs in satisfactory clinical condition with high potential of growth by 10.6% and young kids – by 8.6% and reduce the number of lambs in unsatisfactory clinical condition with low potential of growth by 11.1% and kids – by 5.4%, decrease in the incidence of the lambs by 9.5% and young kids by 7.4% and lethality respectively by 7.5% and by 4.2%, and the number of animals with intranatal (genera hypofunction) and postnatal pathology 13.5% and 8.2% in sheep, 14.4% and 8.7% in goats.

The use of "Carafest" in the complex program for the prevention of perinatal pathologies allows increasing the number of lambs in satisfactory clinical condition with high growth potential by 12.2% and young kids by 8.8% and reduce the number of lambs in unsatisfactory clinical condition with low growth potential by 12.9% and kids by 5.9%, decrease in the incidence of the lambs by 11.1% and young kids by 7.9% and lethality respectively by 8.2% and 5.9%, and the number of animals with intranatal (genera hypofunction) and postnatal pathology by 14.8% and 8.8% in sheep, by 16.1% and 9.7% in goats.

Complex therapy of males with lower reproduction ability using "Carafand" positively influenced the sexual reflexes and sperm quality, due to the stimulation of Leydig cells by androgen-like substances the androgenesis intensified: in bulls – 4.7 times, in boars in 5.5 times and in dogs – 4.9 times; increased the volume of the ejaculate in bulls by 28.2%, in boars by 23.1% and in dogs by 36.1%; increased spermatozoa mobility: bulls – 6%, boars – 16.4% and dogs by 22.8% and the sperm concentration: bulls – 17.1%, boars – 4.4% and dogs by 45.1%; increased percentage of moving spermatozoa in the ejaculate: bulls – 56.8%, boars – 61.3%, dogs 2.1 times; decreased the number of spermatozoa of morphological anomalies: bulls – 2.2 times, boars – 1.2 times and dogs – 1.72 times.

## DISCUSSION

The development of phytodrugs is caused by the search for new drugs, harmless for the body, that have the physiological direction of action. For example, in cattle, in many ways, this is due to requirements that impose the milk quality, limiting the use of antibiotics and hormonal drugs of synthetic origin. A significant amount

of phytodrugs are close to the body of animals in their chemical nature, they are easily absorbed and included in biochemical processes. Biologically active food supplements based on natural phytodrugs are most effective for increasing resistance, stabilisation of the metabolic processes, and improvement of the herd. The basis of phytotherapy is regulatory principle – support and mobilisation of various autoprotection systems: endocrine, immune, the implementation of therapeutic action of endogenous metabolites [33].

M. Kamatenesi-Mugisha and H. Oryem-Origa [45] described 33 medicinal plants that belong to 25 families and 30 genera and are used in traditional medicine in Uganda for the treatment of sexual impotence and erectile dysfunction.

C.H. Browner [46] described the medicinal plants and related substances that are used for stimulation of labor, regulation of fertility, and treatment of reproductive disorders in the indigenous communities of Mexico.

A. Riaz et al. [47] found the positive effects of the drug, which is a herbal combination of *Withania somnifera*, *Tribulus terrestris*, *Mucuna Pruriens*, and *Argyrea speciosa* on fertility in rats of both sexes. The results of the research allow using herbal combinations for sexual dysfunctions, and other disorders of fertility in human medicine.

P.R. Dalsenter et al. [48] conducted a study on the evaluation of the influence of water extract of Yarrow on the reproduction ability of rats. The authors detected a significant increase in the percentage of abnormal spermatozoa in males that received the highest dose, without changes of other indicators of the quality of the sperm. The authors of the predicted estrogen/anti-estrogen activity of Yarrow extract for the treatment of immature rats – females that are not shown ureotrophic effects.

B. Salgado, R. Paramo, and H. Sumano [49] informed about successful treatment of she-dogs pyometritis using the Chinese herbal drug yun-nan-pai-yao.

P. Amato, S. Christoph, and P.L. Mellon [50] studied the estrogen activity of herbs as drugs for the treatment of menopausal symptoms and found a positive effect of dongquai and ginseng and did not establish this in black coughing and licorice root.

E.K. Nwangwa [51] investigated the effect of ethanol extract of *Xylopiya aethiopica* on reproductive status in rats. The results showed a significant and dose-sensitive reduction of morphological characteristics of the testes and sperm parameters (amount, mobility) and a slight decrease in the percentage of spermatozoa with normal morphology. The author concludes that the extract may have some antieffects that can be further investigated for possible use as a male contraceptive.

The task of the research of S. Naser et al. [52] was to determine the effects of alcohol extract of *Physalis alkekengi* on the morphostructure of testes, sperm, and hormone levels in male mice. The extract had an antispermatic

action, showing a decrease in the number of sperm, their activity, and the increase in the number of abnormal reproductive cells, but also adversely affected the level of testosterone, raised the level of luteinizing, and did not change the level of follicle-stimulating hormones. The author concluded that alcohol extract of *P. alkekengi* may be helpful in the regulation of spermatogenesis and the fertility of males.

In the work of N. Malviya et al. [53], the scientific substantiation of the traditionally used herbal plants like herbs aphrodisiac for the treatment of erectile dysfunction sexual disorders was considered. All investigated plants showed significant pharmacological activity. The author believes that herbs can be an effective aphrodisiac, moreover, separation and identification of active ingredients from plants can provide dynamic changes in the modern world.

The number of works related to the use of phytodrugs for the treatment and prevention of reproductive pathologies of animals is limited. In particular, N.Ju. Terenteva [54] has improved preventive measures for postpartum pathology in high-producing dairy cows through the use of phytodrugs and scientific justification for their use. The effect of extracts of herbs nettle and pastoral handbags on the contractile function of the uterus was studied. It was found, that phytodrug of nettle provides fast recovery of the tone of nervous-muscular apparatus of the uterus, helps to normalise the metabolism and increase the activity of the immune system of cows and a total propagation completion of involuntal processes of reproductive organs, prevents the development of subinvolution of the cervix and acute postpartum endometritis, increases fertilisation, shortens the days of infertility.

D.S.H. Habib [55] conducted an assessment of the effectiveness of the original phytodrugs of wood origin (based on the coniferous paw, the bark of willow, and aspen) to stimulate the metabolism and reproductive function of cows. In the end, an effective method of stimulation of metabolic activity and reproduction ability of cows was designed for use in veterinary practice. The author argues, that drugs created by nature, during a long evolutionary development, are more easily absorbed by the body, have softer physiological action compared to synthetic analogs, and are stripped of their harmful side effects.

There are many more examples of the use of drugs with the placenta. They were used for centuries as a folk medicine, especially in Asian countries [56]. Relative to placenta extract, this method is based on the assumption that the extract contains a significant number of so-called biogenic (natural) stimulants (peptides, amino acids, etc.), which have the properties of growth hormone and the ability to activate the metabolism [57]. Since the 30-ies of the last century, methods of preparation and the suspension of the placenta were introduced [58]. In the 1960s-1970s, the effectiveness of human placental drugs

in the treatment of some forms of threatened abortion was studied [59; 60]. The role of the placenta in maintaining pregnancy was shown. In some works, the effectiveness of placental preparations in the treatment of climacteric symptoms was considered.

A number of placental drugs such as PDE, VCP, PAN, "Placentin", "Horiograf", "Placentol", "Umbilicen", "Horiocen", "Amniocen", "Biostimulgin", "Neogistol" [61] are known in veterinary medicine. It is found, that the placental drugs in the maximum doses for experimental animals (mice, rats, Guinea pigs, rabbits) do not cause toxic effects and do not have side effects on the body of the animal, even during their prolonged use [62].

A.M. Semivolos et al. [63] showed that the use of biologically active tissue drugs is of great importance since they allow increasing the natural resistance of the organism of animals and normalise their reproductive function. It was found, that the tissue drug "Placentin", which is a liquid substrate from the cow placenta, stimulates peptide-forming processes, improves the morphological composition of the blood, causing positive changes in the dynamics of total protein and its fractions.

A.G. Narizhnyj et al. [64] when using biogenic stimulators (PDE preparations (placenta denaturalised emulgated) and "Horiocen") for boars-breeders the improvement of qualitative and quantitative indicators of sperm and increase in fertilisation was found. O.S. Mitjashova, I.V. Gusev, I.Ju. Lebedeva [41] established that the introduction of cattle placenta extract to firstborn cows prior to and during calving detects modulating effects on metabolic processes in the postnatal period. The introduction of the placenta also causes the increase in luteal activity of ovarian, which indicates the stimulation of postnatal anestrus. According to the authors, normalisation of the metabolic and hormonal status of cows, obviously, is associated with increasing the reproductive ability of animals and leads to a reduction in future service periods.

O.B. Djachenko, O.I. Stadnycka, L.V. Ferenc [39] argue, that the introduction of the aloe extract and denaturated and emulgated placenta to cows of highly- and low-productive groups, improves the peptide-synthesis liver function, as well as stimulates the nonspecific resistance of their body, due to the activation of humoral immunity. The content of total protein increases, mainly, due to the albumin and  $\gamma$ -globuline fractions. Application of aloe extract and denaturated and emulgated placenta to cows, in the period prior to calving, provides complete recovery of reproductive cycles, increasing fertilisation and reducing the service period.

In general, it should be noted, that the use of placenta drugs with therapeutic and preventive purposes for reproductive pathologies of animals, is limited. In addition, the placenta is used primarily in the form of a suspension (emulgated), whereas, drugs developed by the authors contain its extract, which provides a specific orientation of actions.

## CONCLUSIONS

Thus, vitamin-hormone phyto- and tissue drugs developed by the authors are highly effective for the treatment and prevention of reproductive pathologies of various species of animals, providing the stimulation of reproductive functions therapy for gonadopathies of females, increasing vitality, prevention of the incidence of intra- and postnatal and andrological pathology.

In particular, drugs “Carafest”, “Caplaestrol” and “Caplagonin” are effective in the program of complex therapy of cows, sheep, and goats with gonadopathies in terms of estrus from the beginning of treatment and fertilisation.

The use of “Caplaestrol” and “Carafest” in a comprehensive program for the prevention of perinatal pathologies can improve the clinical condition and development potential of lambs and kids, reduce their morbidity and mortality, as well as the number of sheep and goats with intranatal and postnatal pathology.

A comprehensive program of therapy for males (bulls, boars, and dogs) to reduce the reproductive capacity with the use of the drug “Carafand” helps to stimulate the display of sexual reflexes and improve sperm quality.

In the future, it is planned to improve the developed drugs to provide antioxidant properties by adding nanobiomaterials, in particular cerium dioxide and orthovanadates of rare-earth elements.

## ACKNOWLEDGMENT

The authors express their gratitude to those, who have not joined the article author board, but took part in the development, testing, and implementation of vitamin-hormone phyto- and tissue-based drugs – to the Department of veterinary reproductive and educational-practical complex of livestock and crop production of Kharkiv State Zooveterinary Academy, to the laboratory of reproductive endocrinology of State Institution “V. Danilevsky Institute for Endocrine Pathology Problems of the NAMS of Ukraine” (Kharkiv) and laboratory for aerosole control, disinfectants and antigelminths of State Scientific-Research Control Institute of Veterinary Medicinal Products and Feed Additives (Lviv), as well as the veterinary service of the Vershyna State local hospital of veterinary medicine of Zaporizhzhya region and Svatove district State Hospital of veterinary medicine of Luhansk region.

## REFERENCES

- [1] Commission Directive 91/412/EEC laying down the principles and guidelines of good manufacturing practice for veterinary medicinal products. *Official Journal L 228*, 70-73. (1991, July). Retrieved from [https://ec.europa.eu/health/sites/default/files/files/eudralex/vol-5/dir\\_1991\\_412/dir\\_1991\\_412\\_en.pdf](https://ec.europa.eu/health/sites/default/files/files/eudralex/vol-5/dir_1991_412/dir_1991_412_en.pdf).
- [2] Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products. *Official Journal L 311*, 1-66.
- [3] Kotsyumbas, I.Ya., Bisyuk, I.Yu., Horzheyev, V.M., Malyk, O.H., Zhyla, M.I., Kosenko, Yu.M., Chaykovska, O.I., Muzyka, V.P., Kotsyumbas, H.I., Patereha, I.P., Mazurkevych, A.Ya., Levytskyi, T.R., Brezvyn, O.M., Kushnir, I.M., Perih, Zh.M., & Ivaniv, M.I. (2013). *Clinical studies of veterinary drugs and feed additives*. Lviv: TOV Vydavnychyj dim “SAM”.
- [4] Polova, Zh.M., & Nazarkina, V.M. (2017). The analysis of economic availability of veterinary preparations in the segment of anti-mastitis medicines. *Social Pharmacy in Health Care*, 3(3), 35-41.
- [5] Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (Text with EEA relevance). (2004, March). Retrieved from <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A32004R0726>.
- [6] Zhyla, M.I., Pyatnychko, O.M., & Shkodyak, N.V. (2016). Quality control of generic veterinary medicinal products. *Scientific Bulletin of Lviv National University of Veterinary Medicine and Biotechnology named after S.Z. Gzhytsky, 18(1)*, 36-42.
- [7] Hafez, E.S.E., & Hafez, B. (Eds.). (2013). *Reproduction in farm animals*. Hoboken: John Wiley & Sons.
- [8] Hunter, R.H.F. (1980). *Physiology and technology of reproduction in female domestic animals*. London – New York: Academic Press.
- [9] Yablonsky, V.A. (2004). *Biotechnology of reproduction of animals*. Kyiv: Aristey.
- [10] Klein, B. (2013). *Cunningham's textbook of veterinary physiology-e-book*. Amsterdam: Elsevier Health Sciences.
- [11] Reshetnikova, N., Eskin, G., Kombarova, N., Poroshina, E., & Shavyrin, I. (2012). Baseline conditions and herd reproduction strategy with the increase of cattle lactation performance. *Dairy and Beef Cattle Breeding*, 4, 2-6.
- [12] Abecia, J.A., Forcada, F., & González-Bulnes, A. (2012). Hormonal control of reproduction in small ruminants. *Animal Reproduction Science*, 130(3-4), 173-179.
- [13] Ajbazov, A.-M.M., Aksjonova, P.V., & Seitov, M.S. (2013). Modern biotechnical methods of directional reproduction of small cattle. *Bulletin of the Orenburg State Agrarian University*, 4(42), 241-242.
- [14] Foote, W.C. (1968). Control of reproduction with or without hormones. In *Proceedings: Symposium, Physiology of Reproduction in Sheep* (pp. 104-135). Stillwater: Oklahoma State University.
- [15] Lamb, G.C., Smith, M.F., & Perry, G.A. (2010). Reproductive endocrinology and hormonal control of the estrous cycle. *Bovine Practitioner*, 44(1), 18-26.

- [16] Mwaanga, E.S., Zdunczyk, S., & Janowski, T. (2004). Comparative study on the efficacy of hormonal and non-hormonal treatment methods in ovarian afunction affected dairy cows. *Bulletin Veterinary Institute in Pulawy*, 48(3), 265-268.
- [17] Nezhdanov, A.G., & Lobodin, K.A. (2015). Reproduction of highly productive dairy cattle: The effectiveness of veterinary control. *Dairy Industry*, 11, 64-65.
- [18] Rathbone, M.J., Kinder, J.E., Fike, K., Kojima, F., Clopton, D., Ogle, C.R., & Bunt, C.R. (2001). Recent advances in bovine reproductive endocrinology and physiology and their impact on drug delivery system design for the control of the estrous cycle in cattle. *Advanced Drug Delivery Reviews*, 50(3), 277-320.
- [19] Brinton, L. (2007). Long-term effects of ovulation-stimulating drugs on cancer risk. *Reproductive Biomedicine Online*, 15(1), 38-44.
- [20] Gray, L.E. Jr., Ostby, J., Furr, J., Wolf, C.J., Lambright, C., Parks, L., Veeramachaneni, D.N., Wilson, V., Price, M., Hotchkiss, A., Orlando, E., & Guillette, L. (2001). Effects of environmental antiandrogens on reproductive development in experimental animals. *Human Reproduction Update*, 7(3), 248-264.
- [21] Meyerson, B.J., & Mona, E. (1977). *Pharmacological and hormonal control of reproductive behavior. Drugs, neurotransmitters, and behavior*. Boston: Springer.
- [22] Walker, C.L. (2002). Role of hormonal and reproductive factors in the etiology and treatment of uterine leiomyoma. *Recent Progress in Hormone Research*, 57, 277-294.
- [23] Cupps, P.T. (Ed.). (1991). *Reproduction in domestic animals*. Cambridge: Academic Press.
- [24] Ginther, O.J. (1992). *Reproductive biology of the mare-basic and applied aspects (2<sup>nd</sup> ed.)*. Cross Plaines: Equiservices Publishing.
- [25] McDonald, L.E. (1980). *Veterinary endocrinology and reproduction (3<sup>rd</sup> ed.)*. Philadelphia: Lea & Febiger.
- [26] Mustafin, R.Kh. (2012). Factors of instability in the reproduction of imported livestock. In *Scientific support for the innovative development of the agro-industrial complex: Materials of the All-Russian scientific and practical conference* (pp. 259-262). Ufa.
- [27] Squires, E.J. (2010). *Applied animal endocrinology*. Oxfordshire: Cabi.
- [28] Woodman, D.D. (1997). *Laboratory animal endocrinology: Hormonal action, control mechanisms, and interactions with drugs*. Chichester: John Wiley & Sons.
- [29] Bahmanpour, S., Talaei, T., Vojdani, Z., Panjehshahin, M.R., Poostpasand, A., Zareei S., & Ghaemini, M. (2006). Effect of Phoenix dactylifera pollen on sperm parameters and reproductive system of adult male rats. *Iranian Journal of Medical Sciences*, 31(4), 208-212.
- [30] Kozyr', V.C., Filipov, Ju.O., & Antonenko, P.P. (2014). Influence of phytopreparations on reproductive function of cows and preservation of calves. *Bulletin of the Sumy National Agrarian University*, 7, 147-149.
- [31] Lam, Y.W.F., Huang, S.-M., & Hall, S.D. (2006). *Herbal supplements-drug interactions: Scientific and regulatory perspectives*. New York: Taylor & Francis.
- [32] Newall, C.A., Anderson, L.A., & Phillipson, J.D. (1996). *Herbal medicines. A guide for health-care professionals*. London: Pharmaceutical press.
- [33] Prytkov, Ju.A., & Varenikov, M.V. (2011). The use of herbal remedies for the normalization of reproductive function in cows. *Achievements of Science and Technology of the Agro-Industrial Complex*, 10, 49-51.
- [34] Kotta, S., Ansari, S.H., & Ali, J. (2013). Exploring scientifically proven herbal aphrodisiacs. *Pharmacognosy Reviews*, 7(13), 1-10.
- [35] Pallavi, K.J., Singh, R., Singh, S., Singh, K., Farswan, M., & Singh, V. (2011). Aphrodisiac agents from medicinal plants: A review. *Journal of Chemical and Pharmaceutical Research*, 3, 911-921.
- [36] Sandroni P. (2001). Aphrodisiacs past and present: A historical review. *Clinical Autonomic Research*, 11, 303-307.
- [37] Yakubu, M.T., Akanji, M.A., & Oladiji, A.T. (2005). Aphrodisiac potentials of the aqueous extract of Fadogia agrestis (Schweinf. Ex Hiern) stem in male albino rats. *Asian Journal of Andrology*, 7, 399-404.
- [38] Bagmanov, M.A., Gorshkova N.V., & Hisamutdinov, A.G. (2016). Toxicological evaluation of the biogenic stimulant of the preparation of the placenta extract with germs ("EPL"). *Scientific notes of the Kazan State Academy of Veterinary Medicine named after N.E. Bauman*, 225(1), 14-17.
- [39] Djachenko, O.B., Stadnyc'ka, O.I., & Ferenc, L.V. (2016). Influence of tissue preparations on the parameters of protein metabolism and reproductive function of cows of different milk production. *Foothill and Mountain Agriculture and Animal Husbandry*, 59, 189-198.
- [40] Harenko, M.I., Chekan, O.M., & Harenko, A.M. (2013). Biotechnological measures for the reproduction of pigs and the prospects for their application. *Scientific and Technical Bulletin*, 109(1), 298-302.
- [41] Mitjashova, O.S., Gusev, I.V., & Lebedeva, I.Ju. (2017). Substance metabolism and reproductive function in the postpartum period of the cervix, when administered by the placenta extract. *Agricultural Biology*, 52(2), 323-330.
- [42] Sheremeta, V.I., & Trohymenko, V.Z. (2012). Dynamics of sexual, gonadotropic hormones and biochemical indices in the blood of single cows for the introduction of a drug of metabolic neurotropic action. *Animal Biology*, 14(1-2), 224-229.

- [43] Zakharin, V.V., Kalynovskyi, H.M., & Hryshchuk, H.P. (2016). Biotechnological efficacy of the use of the tissue preparation Fetoplacenate in the maturation of membranes, acute and chronic endometritis in cows. *Bulletin of Zhytomyr National Agroecological University*, 2(1), 205-215.
- [44] Koshevoy, V.P., Ivanchenko, M.M., Skliarov, P.M., Fedorenko, S.Ya., Naumenko, S.V., Besedovskyi, V.P., Onyshchenko, O.V., & Konovalenko, K.S. (2010). Biologically active substances of plants: Development of methods for obtaining from them drugs for use in veterinary obstetrics, gynecology and andrology. *Problems of Zoengineering and Veterinary Medicine*, 21(2), 142-147.
- [45] Kamatenesi-Mugisha, M., & Oryem-Origa, H. (2005). Traditional herbal remedies used in the management of sexual impotence and erectile dysfunction in Western Uganda. *African Health Sciences*, 5(1), 40-49.
- [46] Browner, C.H. (1985). Plants used for reproductive health in Oaxaca, Mexico. *Economic Botany*, 39(4), 482-504.
- [47] Riaz, A., Khan, R.A., Ahmed, S., & Afroz, S. (2010). Assessment of acute toxicity and reproductive capability of a herbal combination. *Pakistan Journal of Pharmaceutical Sciences*, 23(3), 291-294.
- [48] Dalsenter, P.R., Cavalcanti, A.M., Andrade, A.J., Araújo, S.L., & Marques, M.C. (2004). Reproductive evaluation of aqueous crude extract of *Achillea millefolium* L. (Asteraceae) in Wistar rats. *Reproductive Toxicology*, 18(6), 819-823.
- [49] Salgado, B., Paramo, R., & Sumano, H. (2007). Successful treatment of canine open cervix-pyometra with yun-nan-pai-yao, a Chinese herbal preparation. *Veterinary Research Communications*, 31(4), 405-412.
- [50] Amato, P., Christoph, S., & Mellon, P.L. (2002). Estrogenic activity of herbs commonly used as remedies for menopausal symptoms. *Menopause*, 9(2), 145-150.
- [51] Nwangwa, E.K. (2012). Antifertility effects of ethanolic extract of *Xylopiya aethiopica* on male reproductive organ of wistar rats. *American Journal of Medicine and Medical Sciences*, 2(1), 12-15.
- [52] Naser, S., Jasem, E., Maryam, S.L., & Hassan, H.S. (2008). Effects of alcoholic extract of *Physalis alkekengi* on the reproductive system, spermatogenesis and sex hormones of adult NMRI mice. *Pharmacologyonline*, 3, 110-118.
- [53] Malviya, N., Jain, S., Gupta, V.B., & Vyas, S. (2011). Recent studies on aphrodisiac herbs for the management of male sexual dysfunction – a review. *Acta Poloniae Pharmaceutica*, 68(1), 3-8.
- [54] Terent'eva, N.Ju. (2004). *Prophylactic efficacy of herbal remedies in the postpartum pathology of highly productive dairy cows* (Doctoral thesis, Ulyanovsk State Agricultural Academy, Ulyanovsk, Russian Federation).
- [55] Habib, D.S.H. (2017). *Indicators of blood and reproductive function of cows in the use of herbal remedies* (Doctoral thesis, National Research Mordovian State University named after N.P. Ogarev, Saransk, Russian Federation).
- [56] Gromova, O.A., Torshin, I.Ju., Dibrova, E.A., Karimova, I.M., Gilel's, A.V., & Kustova, E.V. (2011). World experience of using preparations from human placenta: The results of clinical and experimental studies. *Plastic Surgery and Cosmetology*, 3, 385-576.
- [57] Harenko, M.I., Homyn, S.P., & Vlasenko, O.A. (2005). *Application of tissue preparations in obstetrics, gynecology and biotechnology of reproduction of animals*. Sumy: Kozatskyi Val.
- [58] Filatov, V.P. (1955). *Tissue therapy (the study of biogenic stimulants)*. Transcript of public lectures delivered to doctors at the Central Lecture Hall of the Company in Moscow (third edition, supplementary). Moscow: Znanie.
- [59] Curone, A. (1967). Placental extracts in the treatment of some forms of threatened abortion. *Minerva Ginecologica*, 19(16), 822-823.
- [60] Rossi, R. (1964). Contribution to the study of the treatment of threatened abortion by means of tissue therapy with placental extracts. *Rivista d'Ostetricia e Ginecologia Pratica*, 46, 136-150.
- [61] Beljaev, V.I., Nezhdanov, A.G., Lobodin, K.A., Semenihih, I.P., & Turenkova, L.T. (2002). The biological activity of drugs from the placenta. *Veterinary*, 5, 33-36.
- [62] Golban, D.M., & Rejljal, N.S. (1990). New tissue preparations for veterinary purposes. In *Collection of scientific papers* (pp. 4-16). Kishinev.
- [63] Semivolos, A.M., Abdrahmanov, T.Zh., Bakbergenova, A.A., & Eszhanova, G.T. (2014). Tissue preparation "Placentin" in the prevention of disease delivery and postpartum period in cows. *Agricultural Scientific Journal*, 5, 24.
- [64] Narizhnyj, A.G., Dzhamaaldinov, A.Ch., Krejndlina, N.I., & Kuripko, A.N. (2013). Application of biogenic stimulants on the basis of tissue preparations to increase reproductive function of boars. *Problems of Veterinary Sanitation, Hygiene and Ecology*, 2(10), 79-82.

## Розробка препаратів рослинного та тканинного походження для ветеринарної репродуктології

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**Анотація.** Сучасні умови практичної ветеринарної медицини вимагають застосування ефективних і безпечних препаратів. Поряд з уже відомими і вживаними лікарськими препаратами необхідний пошук нових, що є нешкідливими для організму і мають фізіологічну спрямованість дії. В останні роки зростає увага до використання препаратів рослинного та тканинного походження, однак проблема їх застосування вивчена недостатньо – багато аспектів їх клінічного використання вимагають подальшої розробки, розширення спектра використовуваних лікарських рослин, обґрунтування і впровадження у ветеринарну практику. Тож мета даної роботи полягала у розробці комплексних вітамінно-гормональних препаратів на основі рослинних і тканинних похідних для лікування та профілактики репродуктивних патологій у тварин. На підставі даних етіопатогенезу порушень репродуктивної функції показників: гомеостазу, зниження концентрації гормонів (естрогену або прогестерону), зміни морфофункціонального стану ендокринних (гіпофіз, щитоподібна залоза та наднирники) і репродуктивних (яєчники) органів, науково обґрунтованим є застосування вітамінно-гормональних препаратів у ветеринарній медицині. Препарати в плані патогенетичної терапії дозволяють оптимізувати показники гомеостазу, концентрацію гормонів, стимулювати реабілітаційні процеси в органах-регуляторах репродуктивної функції (гіпофіз, наднирники та щитовидна залоза) та статевих органах (яєчниках), що, в свою чергу, сприяє нормалізації фолікуло- і стероїдогенезу, які є передумовою для повної репродуктивної здатності самок. Розроблено вітамінно-гормональні препарати на рослинній та тканинній основі, що володіють високою ефективністю за лікування та профілактики репродуктивних патологій різних видів тварин, забезпечуючи стимуляцію репродуктивної функції (прояв ознак еструсу) за терапії самок з гонадопатіями («Карафест», «Каплаестрол» та «Каплагонін») і самців (прояв статевих рефлексів і якість сперми) за порушення відтворної здатності («Карафанд»), підвищення життєздатності новонароджених (збільшення кількості ягнят і козенят із задовільним клінічним станом з високим потенціалом розвитку, зниження їх захворюваності та летальності), попередження захворюваності на інтра- та постнатальну (гіпофункція родів, хвороби післяродового періоду) патологію («Карафест» та «Каплаестрол»)

**Ключові слова:** тварини, самці, самки, новонароджені, репродуктивні патології, лікування, профілактика