

THE EFFECTIVENESS OF USING DIHYDROQUERCETIN (TAXIFOLIN) IN ANIMAL HUSBANDRY, POULTRY AND APICULTURE FOR PREVENTION OF METABOLIC DISORDERS, HIGHER ANTIOXIDATIVE CAPACITY, BETTER RESISTENCE AND REALISATION OF A PRODUCTIVE POTENTIAL OF ORGANISM

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Abstract

The effectiveness of using dihydroquercetin (taxifolin) in feeding cattle, pigs, broilers, hens and bees as a regulator of biological processes in organism in conditions and under impact of technological and environment stress-factors, including pollution by heavy metals (Cd, Pb, Zn, Cu) and radionuclides (⁹⁰Sr, ¹³⁷Cs) was studied. Dihydroquercetin is a natural etalon antioxidant with wide spectrum of biological properties, basic of them being capillary protection with improving blood microcirculation, protection of cells membrane in organs and tissues from destruction by lipids oxidation, support and biocorrection of metabolic health. The introduction of dihydroquercetin in the ration of dairy caws in periparturient period prevented ketosis, improved functional capacity of liver, reproductive ability and herd safety. When using in rations of growing and fattening pigs in extremal environment of high temperature and smog conditions the use of dihydroquercetin prevented lipids oxidation and increased viability of organism that reflected positively on daily gains and safety of pigs. Also positive results were achieved in the application of dihydroquercetin in growing broilers and hens. In beekeeping the use of dihydroquercetin increased reproduction ability of queen bee.

Key words: *dihydroquercetin (taxifolin), cattle, pigs, broilers, hens, bees, environment stress-factors, metabolic health, viability, resistance, safety, animal production, reproduction*

1. INTRODUCTION

The modern livestock and poultry sector is an intensive production of basic food items - milk, meat and eggs, which is based on highly productive genotypes of animals and advanced technology. At the same time, however, the realization of these opportunities are often challenged by poor state of the habitat of animals and poultry and inadequate technology. In addition, the breeding of animals is focused mainly on achieving productivity and product quality purposes, which significantly attenuates the protective functions of the animal body, developed in the process of evolution of species. As a result, new genotypes of animals and birds are much more demanding on the quality of nutrition, diet composition and range of nutrients, meeting the physiological needs of the organism.

Cattle-breeding farms often incur significant losses due to poor maintenance of livestock and poultry, loss of their productivity and reproductive capacity as a result of metabolic disorders stemming from an imbalance of nutrients or shortage of natural essential factors regulating homeostasis, as well as impact of technological and environmental stress factors of abiotic and biotic nature (Donnik and Smirnov, 2001)

For example, in dairy farming by increasing the productivity of cows from 6,000 to 10,000 kg per lactation the number of cases of mastitis cows disease, endometritis, ovarian cysts, maternity paresis, retention of placenta and nipples disease significantly rose (Bloun and De Poo, 2009, Bollwein, 2010, Koelmann, 2011). The rate of culling cows for reasons of metabolic disorders went up by more than 50%. Almost all high-yield dairy cows suffer from ketosis of varying severity, which is the main reason for their removal from the herd at the age of 1,5-2,5 lactations. Among non-contagious animal diseases more than 90% is accounted for diseases associated with metabolic disorders due to an unbalanced diet (Suryasathaporn and Heuer, 2000, Overton and Waldron, 2004).

In recent decades, there have been significant changes in such intensive industries as the livestock, pigs and poultry breeding.

New genotypes of pigs of high genetically provided productivity potential have been introduced, which are intended for intensive production of pork. Meat yield in carcass weight as compared with 1960-s increased by 37%. However, the selection of animals with highly intensive growth leads to the formation of genetically fixed types of animals of late morphofunctional maturity, causing problems of insufficient maturity of their immune system. This problem is exacerbated by the fact that new industrial breeds are very sensitive to stress, especially to high temperatures, which creates a threat to the animals' immunity. Along with the change in the genotypes of pigs requirements to the meat quality have changed, first regarding safety (lack of contaminants - antibiotics, hormones, heavy metals, pesticides and others), as well as such new characteristics as atherogenic index, thrombogenicity index and resistance to oxidation (Chernucha et al., 2009)

Problematic diseases of chickens are technological and thermal stress, fatty liver, which lead to a rapid loss of egg productivity, as well as salmonellosis. In the conditions of cage inactivity, with constant violations of feeding technology, combined with micro-climate issues liver is the first to be affected among the body organs, it increasing by 30-60% when the syndrome of obesity is observed, its consistency becoming very loose. Mortality in the syndrome of fatty liver is more common among chickens with high egg productivity. It is believed that the selection of birds on high egg productivity can be one of the sensitivity factors to a genuine syndrome of fatty liver. This is due to the fact that the high intensity of egg production stimulates fat deposition in the liver accompanied by intense estrogen metabolism. It is believed that fatty liver syndrome arises as a result of stimulation of lipogenesis in layers due to changes in hormonal status.

In the intensive production conditions animal health is most often supported by the use of antibiotics, which may accumulate in animal products, and therefore pose a risk to human health.

Disturbances in metabolism cause structural changes in all organs and systems of the body and reduce their ability to implement their inherent physiological functions. All metabolic processes take place in the subcellular structures of all organs and systems with varying intensity and, therefore, all disturbances in the metabolism lead to changes in the ultrastructure of cells and their functions. Excessive activity of free radical oxidation and formation of toxic products damage the structural integrity of cells (biological membranes), which eventually results in lower productivity and natural resistance of animals and, in certain circumstances, becomes a primary or secondary pathogenetic factor in the disease development.

In the past two decades, according to the WHO, the problem of antimicrobial resistance arising due to unnecessary use of antibiotics in animal husbandry and healthcare is a growing threat. The WHO report of April 30, 2014 for the first time covers more than 114 European and African countries. Feed antibiotics are widely used to stimulate the growth of farm animals and protect them from diseases. However, the use of antimicrobials in large animal populations can lead to the spread of bacteria resistant to antibacterial agents, and cause the emergence of drug-resistant infections. The problem is even more acute in the case of breeding stock.

Providing people with ecologically safe food is one of the priorities in human ecology. Currently, in many countries of the world the formation of the market for ecological (alternative) agricultural products is underway, which guarantees the customer a high quality in compliance with the requirements, in particular, in animal husbandry, feeding and the system of keeping animals which are based on production using natural substances and natural processes (COM (2007) 872 final, 2008/0002 (COD), GOST R 56508-2015).

2. GENERAL INFORMATION AND BIOLOGICAL PROPERTIES OF DIHYDROQUERCETIN

Dihydroquercetin (DHQ, also known as Taxifolin) is a powerful natural antioxidant and capillary protector relating to bioflavonoids with P-vitamin activity. As a substance having a high degree of biological activity DHQ has a whole range of positive (pleiotropic) effects on metabolic reactions and dynamics of various pathological processes that were identified in numerous studies of Russian and foreign scientists, in particular, regarding its antioxidant, radioprotective, membraneprotective,

capillaryprotective, angioprotective, lipid-lowering, anti-inflammatory, antiallergic, cardioprotective, hepatoprotective, detoxification, neuroprotective, gastroprotective, immunomodulatory, retinaprotective, endokrinological effects. It prevents stress and chronic fatigue syndrome, restores and improves performance at high physical and psycho- emotional stress (Plotnikov et al, 2005).

Recognized as a reference antioxidant, it is widely used in medicine and food industry. DHQ is currently used in 104 biologically active additives to food and medicines, as well as in cosmetic products, which are subject to oxidation processes. It is also required for animals, especially when breeding of farm animals and livestock production takes place in areas contaminated with anthropogenic heavy metals (Pb, Cd, As, Hg, and others) and radionuclides (^{90}Sr , ^{137}Cs) or exposed to pollution by industrial enterprises of the chemical, metallurgy, petrochemical and other industries.

Thanks to capillary strengthening and antioxidant properties of DHQ the metabolism on the border of cells and capillary significantly improves and the antioxidant status of the organism is corrected.

The antioxidant action of DHQ, like that of other flavonoids, is a non-specific mechanism for the implementation of many of its other biological properties.

DHQ is a reference antioxidant. Its antiradical activity is shown at a concentration of about 0,0001-0,00001 % in the absence of mutagenic activity.

Antioxidant activity (ORACHidro) of DHQ of 95 % purity is 19,925, that of 80-90% purity is 15,155, while for other popular antioxidants it is 12,500 for luteolin, 10,980 for quercetin, 8,10 for epicatechin, 2,100 and 1,300 for vitamin C and vitamin E correspondingly.

Antioxidant activity DHQ arises from the ability of groups gidrolnyh hydrogen donating molecules, that is donate hydrogen atoms at the developing reaction with the free - radical oxygen metabolites resonance stabilized phenol radical. DHQ functions as an effective "chelator" binding transition metal ions, including stimulating the processes of peroxide, whereby an effective inhibitor DHQ metal catalysed peroxidation of lipids, proteins, nucleic acids and other compounds. By the same mechanism DHQ protects against oxidation and ascorbic acid (Plotnikov et al, 2005).

DHQ is one of the most effective capillaryprotectives. It improves microcirculation direct effect on elasticity, permeability and stability of the vascular walls of the capillaries. A positive effect on blood clotting - reducing its viscosity, facilitates the delivery of oxygen to tissues by improving the ability of red blood cells that carry oxygen to penetrate into the most distant point of bloodstream and affect the level of cholesterol in the blood.

"Ekostimul-1" (hereinafter referred to as DHQ 1) and "Ekostimul 2" (DHQ-2)" feed additives (FA) are designed to improve the productivity and safety of farm animals, including poultry, produced by Ametis JSC.

DHQ 1 contains 1.0-2.0% of DHQ natural bioflavonoid and pulp of Dahurian larch (*Larix dahurica* Turcz) butt and water no more than 20%. The feeding supplement is a coarse powder of light brown color with a specific smell.

DHQ-2 contains: 77-88% of DHQ natural bioflavonoid, no more than 10% of related bioflavonoids (aromadendrin - 2.0-4.0%, caffeine - 0.5-1.0%, eriodiktiol 0.3-0.7%, quercetin - 0.5-1.0%, naringinin - 0.6-0.9%, kaempferol - 0.3-0.7% , pinocembrin - 1.2-1.7%), the balance being of water.

Both feed additives do not contain genetically modified products.

"Ekostimul-1" and "Ekostimul-2" and DHQ-2 " are registered by the Rosselkhoz nadzor supervisor authority under PVR-2-9.9 / 02501 and PVR-2-9.9 / 02502 codes respectively. Dihydroquercetin ($\text{C}_{15}\text{H}_{12}\text{O}_7 \cdot 1.5\text{H}_2\text{O}$) is the dominant component of the Diquertin bioflavanoid complex.

Introduction of the DHQ-2 to feeding farm animals and poultry has a positive effect on immunodeficiency, broncho-pulmonary disease and disorders in the functional state of the liver and others organs, which are usually a consequence of the impact of unfavorable factors of the environment and technology, inadequate for farm animals physiology.

The use of DHQ as a feed additive for livestock produced a positive effect in improving the productivity, safety, reduction of cases of animal disease, normalization of metabolic processes in the body, the functional state of the liver.

3. THE USE OF DHQ-1 IN THE ANIMAL HUSBANDRY FOR INCREASING PRODUCTIVITY AND PRODUCT QUALITY

3.1. Studies on cattle

■ The study of the effectiveness of the DHQ-1 on dairy cows of black-white breed was carried out on experimental farms located on territories with different ecological conditions: one in Moscow region ecologically –relatively well be, another in Tulas region is polluted with radionuclides (RN) and heavy metals (HM) and next in Brynsc region -is polluted RN as result of androgenic factors, including Chernobyl accident.

In Moscow reagon at the "Dubrovicy" farm experimental cows were fed for 30 days with a diet of DHQ-1 at a dose of 10 g and 30 g per head per day. Studies have shown that the inclusion in the diet of cows of 10 g of DHQ-1" per head per day almost did not have any impact on the average milk yield and quality characteristics of milk. When fed at 30 g / head per day average milk yield increased by 10.6% compared to baseline at similar quality characteristics of milk.

At both doses the content of ketone bodies in milk decreased by mg 1,16-0,8% at feeding 10 and 30 g of ' DHQ-1 ', respectively, while the content ketobodys in milk had been increasing in cows of the control group.

A similar pattern on the content of ketone bodies in the blood was observed in cows

Application of "Ekostimul-1" in both doses in feeding cows led to lower blood cholesterol by 0.71 and 0.4 mg % in contrast to its increase in the blood of the control group cows.

The activity of serum ALT in the test period in all cows decreased compared to baseline. Moreover, the decline was more significant in the experimental group of cows, which indicates an improvement of the functional state of the liver.

Clinical and physiological indicators of blood serum of cows on the farm of the Tula Agricultural Research Institute differed somewhat from those of the "Dubrovitsy" cattle farm, which is related to their productivity and the impact of man-made environmental factors, pollution by radionuclides and heavy metals. However, the patterns of their change under the influence of the "DHQ -1" were also observed. The functional state of the liver in experimental groups of cows increased somewhat, but remained within the physiological norm. At the same time two fold reduction in serum of direct bilirubin is the evidence of effective utilization of bilirubin and its excretion into the intestine in bile.

■ In experiments on cows made at farm on Tula region sorption capacity of "DHQ -1" was studied when it was fed at the dose of 10 and 30 g / head / day.

The total content of HM (mg) and ¹³⁷Cs (Bk) in the daily feed ration was 533, 25,4, 76,6, 366,9 and 846,7 correspondingly.

When giving DHQ-1 to cows Cd concentration in their milk increased significantly that shows its probable endogenous origin while concentration of other HM - P1, Cu and Zn decreased, and the content of ¹³⁷Cs was at MDA that can be connected with both decreased endogenous proceeds as a result of adsorption in the gastrointestinal tract of DHQ-1, and its excretion out of the organism in the feces). When "DHQ-1" was given to cows at a dose of 30 g / head / day ¹³⁷Cs concentration grew 2.5 times, and that of Cd was slightly higher than at a dose of 10 g / head/day/. Increased concentration of Cu and Zn in the feces also was noted and that of P1 reduced, which may be associated with specificity of the sorbent and the biological effect of the DHQ-1 on the P1 suction process.

■ The study of the influence of feeding "DHQ -1" on the functional activity of the cows natural resistance mechanisms and ¹³⁷Cs excretion with milk was carried out at the experimental farm . After the Chernobyl

accident radical improvement of pastures with a mixture of sowing grasses was carried out. According to the principle of paired analogs two groups of cows of black-motley breed with an average daily productivity of 10-11 kg with 6 heads in each were formed. The animals welfare was in line with the veterinary and zootechnical requirements. The experiment was conducted during the summer grazing period for 60 days, besides the test animals were fed daily with 2 kg / head of concentrates, and cows of the experimental group got 50 g / head of "Ekostimul-1" in addition.

The cows haemogram shows that most of the indicators are consistent with the values of the physiological norm. Note the reduced level of stab neutrophils and increased for segmented ones in the peripheral blood. This indicates a shift degenerative of the nuclear formulas of these cells due to lack of functional activity of bone marrow. Furthermore, it was found too high blood levels of eosinophils in animals. Given the planned ongoing deworming, this is indirect evidence of reduced functional activity of the adrenal cortex.

In the blood of cows in both groups showed a significant number of lymphocytes with the deformed core, with fragmentation mainly, which is a stage of apoptosis. This type of pathology is almost not found in blood lymphocytes of animals kept in areas with soil contamination density below 1 Ku / km², but appears at a higher contamination.

In cows fed with the DHQ-1, there was a tendency that the hemogram indices got closer to the values of the physiological norm.

The results of studying the effect of the DHQ-1 on the absorption capacity of blood neutrophils in dairy cows indicate that conformity phagocytic index, phagocytic index, phagocytic phagocytosis and absolute numbers in the basal state correspond to normative values. However, adaptation reserve of the absorptive capacity of neutrophils in the blood of dairy cows of the experimental group, which is judged by the degree of increase of blood neutrophils ability to absorb foreign material after introduction to a blood sample of zymosan, was significantly lower than the standard values. In cows fed with FA, there was a trend to the approximation of the indicators characterizing the ability of blood neutrophils to absorb foreign material, to the values of the physiological norm.

The results of the study on the impact of DHQ-1 on microbicidal ability of neutrophils in the blood of dairy cows indicate a very low activity of oxidase enzyme systems in the basal state. After introducing zymosan into a blood sample that simulates a bacterial infection, the activity of these systems of blood neutrophils increases to some extent, but does not reach optimal values, which are: up to 80% - the number of NBT positive neutrophils and more than 1.5 - index of neutrophil activation.

The coefficient of metabolic activation of neutrophils of blood in the experimental cows matched normative values.

In cows treated with DHQ-1, there was a trend to the approximation of the indicators characterizing oxygen-sensitive microbicidal activity of blood neutrophils to the values of the physiological norm.

The oxygen-independent microbicidal activity of blood neutrophils, which are judged by the level of cationic proteins in these cells in animals of both groups did not differ.

Thus the experimental cows in the farm, at which density of soil contamination with radioactive cesium was 15-40 Ku / km², showed strained homeostasis mechanisms, as indicated by the discrepancy of leukogram indicators with normative values (presence of a significant number of lymphocytes with fragmented nucleus, low level of stab neutrophils and high level of eosinophils).

The ability to absorb and destroy foreign material by blood neutrophils in the basal state of the experimental cows corresponded to standard values, and the adaptation reserve of these mechanisms was significantly lower. Inclusion of the DHQ-1 in the diet of lactating cows reduces excretion of ¹³⁷Cs with milk 1.45 times and were 15,68 in experimental caws and 22,77 Bk/kg in control.

Reduced ¹³⁷Cs content in milk is due to the influence of the FA on metabolic rate and its ability to adsorb radionuclides in the gastrointestinal tract, thereby decreasing their absorption.

Thus, the feeding of cows with 50 g / head of the FA "Ekostimul-1" for 60 days has caused a marked tendency of the optimization of the blood pattern, increased functional activity of the body's natural resistance mechanisms and reduction of the content of ^{137}Cs in milk of lactating cows by 1.45 times.

■ A study of the influence of the DHQ-1 on the sorption of ^{137}Cs and ways of its elimination from the body was held at the "Rodina" agricultural production cooperative in the Novozybkov district of the Bryansk region affected by radiation contamination as a result of the Chernobyl accident. The aim of the study was to investigate the impact of the DHQ-1 on dairy cattle productivity.

For the experiment, according to the analogue pairs principal two groups of multiparous cows black-and-white breed with an average daily productivity of 11 - 12 kg. The experiment was conducted during the summer grazing period for 60 days.

Studies carried out in the "Rodina" cooperative has shown that the inclusion in the diet of 250g / head / day of zeolite and 50g / head / day of DHQ-1 has a positive effect on the milk production of cows

Excretion of ^{137}Cs with milk in the cows of the experimental group decreased in comparison with the control one by 5,8 Bq / kg. This accumulation rate also decreased by 1.3 times. During the research it was found that the inclusion in the diet of cows of the FA has a different effect on the removal of ^{137}Cs from the body with milk, feces and urine

Withdrawal of ^{137}Cs with milk, feces and urine from the body of different groups of animals differed. In the control group 24% of the total radioactivity was withdrawn with milk, 45% in the feces, and 31% with the urine. In cows of the experimental group ^{137}Cs excretion was respectively 16%, 59% and 25%. It was observed that in the experimental group the amount of the ^{137}Cs excreted with the milk was 1.1 times smaller, and that in the feces 1.87 times greater than that in the control group of cows. The excretion of ^{137}Cs with urine in the cows receiving DHQ-1 was 1.16 times higher than in the control group. As a result, the total excretion of ^{137}Cs in the test group of cows was 1.5 times larger than that in the control group of cows. Thus, the inclusion in the diet of DHQ-1 in an amount of 50 g / head / day prevents absorption of radionuclides in the gastrointestinal tract/ reduces the excretion of ^{137}Cs with milk and increases its excretion with urine. Feeding cows with FA "Ekostimul-1" also contributes to an increase in milk production and milk fat.

■ In an experiment on calves of dairy rearing period conducted at the experimental farm of Tula region dosage of the DHQ-1 the feeding milk has been studied.

Two dosages were tested: 5 g and 10 g per head per day. The results showed that the dose of 5 g / head / day was more preferable than 10 g / head / day.

Visible advantages in the growth of calves within two months of feeding DHQ-1 with regard to the control calves was not observed. The average increase during the experiment was 503-550g and 396-476 g, when fed 5 and 10 g of DHQ-1, respectively, and 480 - 563 g in the control group. However, over the next three months follow-up after the termination of the experiment the daily gain in calves of the first test group was 1200, 1016, and 1080 g, in the second test group - 1119, 993 and 1206, while in the control calves it was slightly lower and amounted to 1132, 763 and 1167 g by months. These data may indicate that the use of DHQ-1 increases the viability of young organism that determines its stability also in there later lifetime.

Studies have shown that "DHQ 1" has an active cationic capacity, it can be used in technological areas as enterosorbent in the elimination of HM- copper, zinc, lead, cadmium and RN- ^{137}Cs and ^{90}Sr .

Inclusion in the diet of calves of 5 g of DHQ-1 per head per day increased excretion of Cu, Zn, Pb and Cd in more than 2 times, while when giving 10 g that was on the average for Cu, Zn and Pb in 1.5, and for Cd - more than 20 times. When an amount of 5 - 10 g per head per day DHQ-1 was included in the diet the excretion in the feces of ^{90}Sr was more than two-fold higher than in the control group. The ^{137}Cs excretion in the feces when giving 5 g of DHQ-1" was higher than in the control animals by more than 5 times, while giving 10 grams - almost 2 times.

The results of these studies indicate the possibility of widespread use of "DHQ -1" in greening the technology of rearing livestock and the livestock production in the technogenic regions of Russia unfavorable regarding HM and RN.

3.2. Studies on pigs

■ A study of the effectiveness of the "DHQ -1" for weaned piglets was carried out on 4 groups of pigs of large white breed after weaning of 60 days of age for 30 days on experimental pig farm of the All-Russia Animal Husbandry Research Institute. The first group was the control one, the 2nd, 3rd and 4th groups of piglets were given with feed DHQ-1 in doses of 1g, 5g and 10g, respectively.

The DHQ-1 was additionally grounded in a laboratory mill to a uniform granular mass, which was added to the feed in the mangers, on a daily basis in accordance with the doses indicated in the experiment schedule. Piglets before and after the experiment were weighed individually.

During the period of experience pigs in all groups ate the feed completely. 100% of animals in all groups have been alive. Cases and disorders of the digestive tract of piglets in the control group, the 2nd and 3rd experimental groups were not observed. In the 4th group when giving 10 g of DHQ-1 per kilogram of feed in two weeks after the start of the experiment there were observed cases of disorders (diarrhea), which lasted for one week. After the reduction of the dose of to 5 g / kg of feed indigestion stopped. Giving the DHQ-1 at a dose of 1 - 5 g / kg of feed was optimal. In both groups there was the average daily increase of 540 g, which was higher by 97 g or 21.8% compared to the control group that was statistically significant at $P < 0.001$.

3.3. Using DHQ-2 and arabinogalactan for the purpose of maintaining productive health and increasing productivity of animals and birds

3.3.1. Prevention of ketosis in high yielding dairy cows

In contrast to raising ruminants, high yielding cows in, particularly in early lactation, as well as in ewes at the last stage of pregnancy ketosis is observed. It represents a metabolic disorder, which is characterized by elevated levels of ketone bodies in the body fluids and a decrease in blood glucose levels.

To the ketone bodies β -hydroxybutyric, acetoacetic acid and acetone relate. Since this metabolic disorders increases not only the content of acetone, but other compounds, it is no longer called acetonuria, but more correctly ketosis instead. Ketosis is most common in high yielding cows.

In order to prevent disturbances of lipid metabolism in the liver and maintain it in a physiologically normal functional state, as well as, provide organism cells with energy a technique of combined use of feed additives has been developed. It prevents ketosis and corrects metabolism in high yielding dairy cows, which provides maintaining health of cows in the dry period and milking and as a result an increase in productivity and safety.

The complex of FA consists of L-carnitine at 15 g / head / day ; choline chloride - 50 g / head / day; and DHQ-2 - 200 mg / head / day, which are introduced to the feed when feeding cows during the two weeks prior to calving, and during the first 100 days of lactation.

The selection and sequence of application of the complex feed additive is based on physiological and biochemical action of its components, taking into account the probable development of hypoglycemia in the body of cows, leading to impaired liver function.

Experiments were carried out on experimental farm "Dubrovitsy" Chegodaevo" Two groups of cows of black and whit breed were selected of 10 heads each, paralleled in terms of calving, productivity and age. The control group received basic diet, experimental one - besides basic diet also L-carnitine ("Carnipas"), choline chloride and DHQ-2.as FA "EcoKor" Application of the complex FA "EcoKor" in the dry and calving periods had a positive effect on the normalization of metabolism and productivity of dairy cows. Study of the metabolic, free radical oxidation of lipids, antioxidant protection of the organism, the functional state of the liver in high yielding cows during the first four months of lactation showed that they were in a state of subclinical ketosis.

The severity and speed of development of the clinical picture is closely associated with a significant increase of ketone bodies in the blood of cows with ketosis. Degree of ketonemia is inversely proportional to the level of hypoglycemia. The study of the content of ketone bodies in cow milk in the control group and their dynamics within 4 months of lactation showed that their total number was higher than the norm and remained practically unchanged throughout lactation months at the ratio of 7.4: 1 ... 8.3: 1. Application of the complex FA in the period before calving and during the 4 months of lactation prevented development of ketosis in cows and resulted in reduction of ketone bodies in milk during months of lactation, mainly due to the β -hydroxybutyric acid with a stable content of acetoacetic acid and acetone for 2nd ... 4th months of lactation.

The same pattern was observed on the content of ketone bodies in the blood. In cows in the control group their content was stable during the first months of lactation, and was equal to 7.1 mg%, while in the cows of the experimental group it was 6.34 mg% in the first month of lactation and 6.06 mg% in the third month of lactation. Blood glucose content plays an important role in the genesis of cows ketosis. Decrease of its concentration is the trigger for gluconeogenesis, when lipids and proteins are mobilized for energy purposes.

In cows of the control group blood glucose level was lower than in the test one, by 1.02 to 0.87 mmol / l at the beginning and in the third lactation month, respectively. This could have an impact on the increase in the content of ketone bodies, which was higher than that of the experimental group of cows by 11.2 and 17.2%. This data are positively corresponded also by the content of the products of free radical oxidation of lipids - malondialdehyde, free fatty acids, peroxide and acid numbers. As a result, the antioxidant activity in the control group of cows was also lower than in the experimental group by 0.64 to 0.32 l ml⁻¹ min⁻¹ 10⁻³.

Normalization of metabolism from the first month of lactation contributed to the maintenance of the lactation curve in a stable higher level for the entire period of observation. According to the control milkings the daily average milk yield in the first 100 days of lactation in the experimental group was 35,0 ± 2,41 kg of milk, and in the control group - 29,3 ± 3,17 kg, resulting in a higher gross yield for this period for cows of the experimental group than in the control one by 561 l/kg or 19.1%.

For 305 days of lactation cows of the experimental group produced 9207 kg of milk, which was 715 kg more than in the control group. Of that 154 kg of milk were received after the termination of giving FA.

Thus, a consistent and comprehensive application of L-carnitine ("Carnipasa"), choline chloride and DHQ-2 in the dry period and during the first three months of lactation has not only prevented ketosis in cows, but also had a positive effect in the subsequent period regarding their productivity with full health safety. At the same time in the control group 4 cows retired due to endometritis disease and bone disease that was caused by ketosis.

3.3.2. Increasing the productivity and viability of young farm animals and poultry

Application of DHQ-2 for growing calves in the dairy season on milk acidified with formic acid has been studied at the JSC "Krasnaya Poyma" in Moscow region.

The study was conducted on 3 groups of calves of black-whit breed in two periods: 1st in age from 15 to 65 days, 2nd - from 66 to 115 days. The calves of group 1 during the 1st period was given with milk acidified with formic acid (MPMK) and vegetable food (OR).

Calves of 2-nd and 3-rd groups were administered with DHQ-2 at a dose of 20 and 40 mg / head / day, respectively.

During the 2nd period the calves of the control group received OR and those of the experimental group in addition with forage got DHQ-2 at 30 and 60 mg / head / day. Overall, during the period of experiment calves of the control and experimental groups consumed on the average 250 kg of MPMK, silage corn - 265 kg, hay - 70 kg, 145 kg of mixed feed.

Analysis of the data on body weight change and average daily gain shows that the effective dose of DHQ-2 in the 1st period was 40 mg / head / day, and in the 2nd - 60 mg / head / day. In this group the

average daily gain increase of the calves in the 1st period of raising was 864 g, and in the 2nd - 1113 g, which was higher than the control group of calves by 13.1 and 10.5% respectively.

Application of DHQ -2 in feeding calves enhanced the anabolic processes in the organism, as evidenced by the higher protein content and, in particular, its albumin fraction (group 2), which corresponds with the average daily gain. Lipid metabolism was studied in calves according to the content in blood of the total lipids, phospholipids, cholesterol and lipid index. The normal serum lipids in cattle fluctuates quite widely from 280 to 600 mg % that is associated with a wide variety of factors, reflecting both feeding diet and condition of individual organs and endocrine glands of an animal.

As a result of the studies, it was found that in 2.5 months the concentration of total lipids and its components - phospholipids, cholesterol in the blood of experimental animals was higher than in the control group (except for a slight reduction in the level of phospholipids in group 3). In the third group (treated with DHQ-2) there was a significant increase in the concentration of total lipids by 44,7% ($P \geq 0,99$), phospholipids - 19,8% ($P \geq 0,95$), cholesterol - 28.6% ($P \geq 0,99$). In the experiment the lipid index in the 2.5 months was approximately at the same level in all groups.

At 4 months total lipid concentration in the blood of calves of the test group was also higher than the control one, except for group 2. The concentration of phospholipids in the 2nd and control group was at the same level, and in the third experimental group there was observed excess of benchmarks. The concentration of cholesterol in all the groups were similar, and that in the third one was higher than in the control group by 9%. The lipid index (in 4 months) had similar values in all groups.

Thus, in general, total content of lipids, phospholipids and cholesterol in both 2.5 months and 4 months exceeded benchmarks that indicates an intensive lipid metabolism in experimental groups of calves.

Blood levels of phospholipid and cholesterol also shows the functional state of the liver, as they come mainly from it. Low blood levels of phospholipids may be indicative of inadequate feeding, imbalance of amino acids and protein-vitamin deficiency. Low cholesterol content is marked when liver function is abnormal. In these studies, blood cholesterol levels in calves was within the physiological range. Alkaline phosphatase activity in blood was the highest in calves receiving DHQ-2 at a dose of 20 and 40 mg / head / day, respectively, in the 1st and 2nd period of experience, and the lowest - in calves fed with the same feed additive, but at 40 and 60 mg / head / day.

Lysozyme activity of blood serum (LASK) of experimental groups of calves at the age of 2.5 months slightly exceeded targets. In 4 months the activity was significantly higher than in the control group by 28.9%. Serum bactericidal activity (BASK) in 2.5 months was significantly higher in calves in group 3 by 27.8%, and 4 hours later the index was significantly higher also in the 2nd experimental group, by 41.8%, and in 2nd - 47%. At the age of 4 months BASK tended to increase (significantly increased after 4 hours) by 7.3% in calves treated with DHQ -2.

■ Symbiotic properties tokokarin and carotinobakterin when combined with DHQ -2 in the enrichment of acidified milk for calves were studied on calves of black -white- breed in the milking period of raising from 15 to 120 days. Rations for feeding calves were developed in compliance with detailed standards of feeding which was performed according to the technique adopted at the farm. Calves of control group received only basic ration with acidified milk with formic acid (BR), calves 1-st experimental group – BR and addition in age 15-60 days tokokarin and carotinobakterin in dose of them each 5 billion and 500 millions cels; calves 2-nd experimental group received the same, but addition DHQ-2 in dose of 40 mg /head/day.

Acidification of milk with formic acid reduced in more than 10 times its overall contamination and completely eliminated the coliform bacteria, mold and yeast. It significantly reduced the number of staphylococci and Enterobacteria ccae, and contributed to their elimination during storage for 48 hours. When storing the acidified milk for the next day these bacteria groups were not detected.

During storage there was a slight increase of the total contamination, which in 72 hours after acidification reached 4.56 th. CFU / ml, which was 1.45 times higher than upon acidification.

Acidification of milk with formic acid resulted in a decrease of lactic bacteria in more than 90 times, which had a tendency to increase during the 72 hours storage.

Adding probiotic cultures in milk along with its acidification had no effect on the conditionally pathogenic microorganisms, yeast and mold, but promoted the growth of MAFAnM and lactic microorganisms by 70 and 35%, respectively, for storing milk for 24 hours.

Applying biocomplex consisting of probiotics and DHQ-2 in milk at its acidification, also contributed to the growth of MAFAnM and lactic acid microorganisms, and the elimination of conditionally pathogenic microflora. These changes in the composition of the microflora of milk as a result of its acidification with formic acid and its enrichment in probiotics and antioxidants indicates an increase in its sanitary and hygienic properties, and safety indicators, it corresponds to pasteurized milk in tanks and jars according to Russian official standards.

When studying the effect of the acidity environment, close to the conditions of the upper gastrointestinal tract of the calf, on the growth of the probiotic cultures studied by us it was found that at pH = 4.01 inhibition zones growth was not detected. It is important that the pH of the milk abomasum acidified with formic acid, has the same value.

In *in vitro* experiments, the milk acidification with formic acid at pH equal to four oppression of viability *tokokarina carotinobakterina* did not happen that can be extrapolated to experiments *in vivo*.

When considering the dynamics of intestinal biocenosis for the entire test period (120 days) as a whole, we find that the population level of the ICD in the contents of the large intestine of calves in all groups increased, while the number of coliforms, enterococci, molds and yeasts decreased compared to the 15-day age. The number of mesophilic microorganisms increased in all groups. The greatest growth in 2.5 and 3 times was detected in the experimental groups 1 and 2, respectively.

The total number of microorganisms in the feces increases calves in all groups. Coliform content in calves of the experimental groups were slightly higher than that in the control group. With age, there is an increase in the number of lactic acid bacteria, and the difference between groups was not significant. Number of staphylococci and enterococci to 4 months of age decreased slightly. Yeast and mold content in feces of calves treated with BAS was lower than in the control group.

Regarding the data of lysozyme activity of blood serum of the experimental groups of calves treated with the complex of biologically active substances for the entire test period, its rise to 60 days of age by 13-13,2% was observed, while in the control group the rate remained at the initial level. By 120 days of age there was a further increase of this parameter in the 1st and 2nd test groups where it was 26,73-27,83%, respectively, while in the control one the lysozyme activity was at 13.35%. The bactericidal activity of blood serum in the test calves 1st and 2nd groups to 60 days of age increased by 1.9 and 1.4 times, respectively, which is 2% higher than the control level. At the age of 120 bactericidal activity in the experimental groups continued to increase and reached 18.9% and 20.98%, while in the control calves remained at baseline.

In calves treated with the probiotic complex and DHQ -2 only in the first period of the experiment there also was an increase in the lysozyme activity to 60 days of age by 6% and 12.7%. In 120 days of age the rate was 20.98% and 24.75%, which is by 5.7% and 3%, respectively, less than in calves that received BAS during the test period. The bactericidal activity of blood serum of calves to 60 days of age in the experimental groups was 12.87% and 15.05% respectively, while in the control one -12.61%. At age of 120 days, the rate increased in the experimental groups by 3.6% and 4.8% respectively, and in the control one by 4.9%.

The findings suggest that indicators of natural resistance were higher in calves that received *tokokarin* and *karotinobaktin* combined with DHQ -2 throughout the experiment. Antioxidant protection of the organism much better formed in calves treated with BAS. In the beginning of the feeding calves peroxides content tended to decrease in the blood serum, and by the 60th and at 120th days of age differences in LPO indices were significant at $P < 0.05$. Inclusion of DHQ 1-2 in the feeding diet increased the antioxidant defense, resulting in significant decrease of LPO indices relatively to the control calves and the experimental group 1. Upon termination of giving BAS to the calves by reaching

60 days of age the advantage of AOP in the experimental calves compared to the control group remained, and it was also the best in calves treated with probiotics together, which can be described as an indirect effect of functional systems of the AOP, which was formed in the early period of ontogenesis.

The content of total protein, albumin and globulin, and urea in the blood serum of calves under the influence of probiotics and antioxidant were within the physiological range. However, between the groups were some differences during the test period. Termination of application of probiotics in the period from 60 to 120 days of age did not have a negative influence on the content of proteins in the blood serum, in fact it was higher in comparison to the control and the group of calves treated with probiotics for 120 days, which may indicate the emergence of and development of the organism's own structures responsible for their resistance.

Analysis of the content of urea in the blood serum indicates that these feed additives do not affect the urea formation processes in the organism (liver, tripe) and its clearance via the kidneys. Its level decreases with age, but was within the physiological norm.

Serum glucose in all groups of calves throughout the experiment was within the physiological range. The total bilirubin, direct and indirect, in the calves serum in all groups was within the physiological range, which is equal to 11.97, 6.84 and 5.13 mol / L, respectively, but between the groups of calves were ontogenetic differences. Termination of probiotics application both separately and in combination with DHQ-2 resulted in a significant increase in the content of total bilirubin, direct and particularly indirect with respect to both the previous level, to the control group of calves and to calves subgroups treated with these additives for 120 days, which may indicate the tension in the detoxification and its excretion from the organism. The activity of ALT and AST in calves of all groups were within the physiological range and close, and the change in the activity was mostly of aging reason.

Inclusion of DHQ-2 in the calves feeding diet enriched with probiotics, amplifies general biological effects on the organism of calves, which allows additionally get daily gain during 120 days of growing calves by 100 g greater than that of the calves of the control group and by 26 g than in the group of calves which received only probiotics. These results are achieved by increasing the metabolic rate and a better utilization of feed.

Application of tokokarin and karotinobakterin separately and in combination with DHQ is effective only at the time they are introduced into the calves feeding diet. However, one can note the tendency of retaining the achieved advantages also in the subsequent period of growth, which results in reducing the incidence of diarrhea and in some advantage in growth rate, as a manifestation of the calves productive health factor

Thus, the milk acidification with formic acid at a concentration of 0.16-0.2% reduces more than in 10 times the total contamination and eliminates completely CGB, molds and yeasts, and on storage for 48 hours - Staphylococcus and enterobacteria.

The inclusion of milk acidified with formic acid, and fodder and tokokarin karotinobakterin alone and in combination with DHQ -2, inhibits the growth of the conditionally pathogenic microflora and stimulates the growth of lactic acid microorganisms in the large intestine of calves. As a result, there is more than two-fold reduction in the indigestion cases per one head.

Application of tokokarin and karotinobakterin separately and in combination with DHQ-2 forms a stable mechanism of non-specific resistance in the first two months of calves raising that upon the exclusion from the diet the feed additives at 60 days remains high in comparison with the control group and the groups of calves treated with probiotics and DHQ-2 for 4 months.

Calves treated with probiotics had significantly lower indicators of lipid peroxidation (LPO). Introduction of DHQ -2 increased the antioxidant defenses of the organism, resulting in decreased LPO indices in comparison to the control group and the group of calves treated with probiotics.

The activity of ALT and AST in calves of all groups were within the physiological range and close, and the change of activity was mostly aging character. However, there was a trend of increase in the activity of both ALT and AST in the calves group receiving along with probiotics also DHQ -2 both for 60 and

120 days, which may indicate from a clinical-biochemical and physiological point of view, a more intensive processes of transamination and normalization of the liver and the heart - cardiovascular system, that may ultimately be assessed as an impact of a positive factor.

Introduction to the diet of feeding calves in the dairy and post-dairy growing periods until the age of 120 days of tokokarin and karotinobakterin alone and in combination with DHQ -2 contributed to achieving the average daily gain during the whole growing period 791 and 817 g, respectively, compared to 717 g in the control group, while reducing the cost of feed in the ECE by 7,8-10% and digestible protein by 8,1-11%. Termination of application of probiotics and antioxidants in the calves feeding in the post-dairy period leads to lower average daily gain to the control group level.

■ Research of influence DHQ-2, probiotics and tokokarina lactoamilovorin organism suckling piglets conducted at a experimental pig farm of institute. Tokokarin asked at a dose of 200-600 million. №100 microbial strain per head per day, depending on age, which corresponded to a dose of 5-15 grams of dry product per group. amilovorina dose was 8.10 ml per head per day. DHQ 2 fed at the rate of 10 mg per 1 kg feed in the form of 0.1% aqueous solution. Were mixed with serum and asked for groups (nests) by method of calculation of 0.5-10 ml per animal, depending on age.

Influence DHQ -2 on mutual antagonistic activity strains №100 genus *Flavobacterium* and *Lactobacillus amylovorus* BT-24/88 has been studied according to the study design , including 4 group; 1-st control, received BR, 2-nd – BR + DHQ-2 and tokokarin, 3-rd – BR + DHQ-2 + amilovorin, 4-th – BR + DHQ-2. In vitro studies on the subject strains antagonistic activity №100 genus *Flavobacterium* and *L. amylovorus* BT 24/88 showed compatibility strains selected for the experiment on pigs. Antagonistic activity with respect to each other in a wide range (10⁻¹-10⁻⁴) concentrations did not show these microorganisms.

The presence of DHQ-2 working concentration of 0.1% and above its order to not affect the growth of these strains and their tolerance to each other. Zones of growth inhibition were not detected in any of the drug combinations tested. It was found that the use in feeding pigs DHQ -2 and probiotic preparations and tokokarina amilovorina combined with DHQ -2 helps reduce the number of digestive disorders and increased average daily gain. For the experimental group, this increase was, respectively, 9.4%, 6.7%, 21.5% and 15.9% of the control value.

The intensity of the growth of the animals increased in all experimental groups. Animals in the 3rd and 4th groups grew better than the control pigs of 21.1% and 16.6%, and the 1st and 2nd - 8% and 7.4%.

This allowed a better use for their growth nutrients intake. Consumption of feed for 1 kg of growth decreased in the experimental group compared with the control group by 8.3%, 6.1%, 17.7% and 13.5%, respectively.

It is found that by using DHQ-2 and probiotics tokokarina amilovorina and coupled with DHQ-2 digestive system disorders were 1,5-2 times less in calculating the head.

Ratio of cases within the first month of observation (pigs aged 10 to 45 days) subsequent to the diseased 2 weeks (at the age of the piglets on days 45 to 60) on average in the experimental groups decreased by 4.4 times, while the control group is a decrease of 1.3 times. In other words, the peak incidence of piglets experimental groups shifted to the 1st half of the experience, and the control group continued to get sick pigs in 1,5-2 months of age.

Among pigs experimental groups between the ages of 10 to 45 days had no advantages in the 2 nd experimental group receiving amilovorin with Ekostimul-2, and the largest decrease in the incidence was observed in group 1 piglets receiving tokokarin with Ekostimul-2 - 35% control below.

After 45 days of age showed a decrease morbidity in the group 2 (amilovorin + DHQ-2), in the third group (probiotics + DHQ -2) and the 4th group (DHQ-2) at 79%, and 1 th group (tokokarin DHQ-2) - 67.2% of control. In young animals the safety margin not seen since none of the groups were not livestock losses during manufacturing experience.

Evaluation correcting probiotic action and DHQ -2 large intestine microflora pigs showed that the number of different groups of microorganisms of the intestinal contents thick card piglets after drug

withdrawal (aged 60 days) compared with the quantitative indices of microflora intestinal contents before the test (at the age of 15 days) and one month after the start of feeding the products (at the age of 45 days) has changed in all experimental groups of pigs. Watched characteristic shift of population levels of different groups of microorganisms in the intestinal contents of pigs in the control group a month feeding of biological products, typical of disbakteriosis.

Also noticeable different degree of influence we study complex preparation (CP) on intestinal biocenosis of experimental groups of pigs. After a month of feeding drugs (CP) in all groups were some increase in the number of mesophilic microorganisms (MAFAnM). The highest growth was recorded in the 1st and 3rd experimental groups - by 3.7 and 3.3 times respectively. The smallest - in the 2nd group of pigs - by 1.3 times. In the control and 4th groups increased total 1,6-1,65 times.

The 1st group of mesophilic aerobic growth was accompanied by an increase of 1.5 times the number of lactic acid microorganisms. The ratio of the ICD to the CGB increased by 1.6 times and amounted to 45 days of age 29 1. Number of staphylococci was not significantly changed, and enterococci increase more than 2-fold increase in the number of yeast accompanied by 1.5 times.

In the 2nd group of pigs treated with amilovorin DHQ-2, there was a significant increase in the number of ICD - 5.7 times. Despite the increase in the CGB number 2 times the ratio between these groups of microorganisms in the first month experience increased from 12.2: 1 to 35.7: 1. The amount of yeast microorganisms group remained almost at the level of primary level.

Signs disbakteriosis changes in the gut of piglets in group 2 was a decrease of 1.2 times enterococci while increasing number of staphylococci by 1.3 times. This age period is characterized by stable state of the piglets on diarrheal diseases character, in percentage against the number of days of pigs diseases Group 2 equalize with that in the control group.

However, the presence of diarrhea in piglets in group 2 had lower rates of refusal of food, oppression, have had illness milder, piglets recovered faster. Status intestinal contents of pigs control group showed an increase in fermentation processes, noted the displacement of bacterial background towards increased number of yeast fungi in crops to identify the growth of yeast groups of microorganisms.

The intestinal contents of 45-day-old piglets Group 3 3-fold increase in the number of mesophilic microorganisms proceeded with changes in relation to ICD CGB 3.3 times due to the significant increase in number lactic acid bacteria. The increase in their number increased by 8.9 times the ratio of the ICD to CGB from 16: 1 to 53.3: 1 for the first month feeding drugs. The growing number of Enterobacterias (coliforms) in 2.6 times was accompanied by somewhat lower growth of enterococci - in 1,5 times. Number of yeasts and molds changed slightly upwards to $1.1 \cdot 10^2$ CFU / g, while the number of staphylococci index remained at the age of 15 days.

The 4th group of significant changes in the number of staphylococci and enterococci was observed. The number of microorganisms remaining groups increased by 1.5-1.7 times in comparison with its level in the intestinal contents 15-day-old piglets.

During the subsequent 2-nedelny period of experience in the age of the piglets from 45 to 60 days microbial landscape of the intestine contents of the thick card changed. By the age of 60 days, there is a restoration of intestinal biocenosis piglets. The intensity of this process differed significantly depending on the BAS, pigs consumed.

Pronounced changes microbiological parameters observed in the control group. Unlike other groups of pigs, where MAFAnM slightly increase or decrease in the amount, controlling the total number of microorganisms increased to 2.6 times. Due to the rapid growth of the ICD (4.4 times) and reducing coliform bacteria (2.5 times), the ratio of representatives of these groups taksonometric group increased more than 11 times (from 0.8: 1 to 45 days of age the piglets to 8, 9: 1 in the 60-day). Reducing Yeast groups of microorganisms in 2.5 times (mainly due to the number of yeasts) also indicate a recovery of the microbial landscape of the intestine of pigs in the control group. Also, there was some increase in staphylococci (1.24 times) and a relatively stable number of enterococci.

The growth of lactic acid bacteria observed in all groups: in the 1st, 3rd and 4th groups - in the 2.1-2.25 times, the 2nd - in 1,2 times. Reducing the Enterobacteries population in the age period was observed in group 2 (other than control). By 60 days of age the ratio for ICD CGB was as follows: in group 1, 54.5: 1, in the 2nd group, 59.2: 1, in the third group of 91: 1, in the 4th group of 36, 2: 1.

If we consider the dynamics of the intestinal ecological community for the entire test period as a whole, it should be noted, the ICD population level in the contents of the large intestine of 60-day-old piglets reached and exceeded the similar value of beginning of the experiment in all groups.

Mesophilic microorganisms are increased in their numbers in the five groups of pigs. The highest growth was detected in the control group - 4.2 times, and the third - 4.6 times.

The relatively low level of the ICD and the relatively high content of bacteria esherihides group (8.9: 1), increasing the number of staphylococci is 1.9 times against the background of reducing the number of enterococci indicatived of instability intestinal biocenosis in the control piglets weaned age. The growth of the total number of microorganisms more than 4 times was mainly due to the representatives of conditionally pathogenic groups.

In the third group, which was fed DKV in conjunction with probiotics, the number MAFAnM experience for the entire period increased by 4.6 times. To a large extent due to lactic acid (18.9 times), enterococci (5.3 times) and CGB (3.3 times). Population staphylococci rate rose by 1.4 times.

In the 2nd group of piglets receiving amilovorin, MAFAnM growth amounted to 1.4 times the number of ICD has increased 6.9 times, 1.4 times CGB, while the ratio of their experience of the period increased by almost 5 times.

The greatest increase in relation to the IBC 50 CGB of days noted in the experimental group 3 - 5.7 times (91.1: 1). This group recorded the largest increase in the number of ICD 1.5 months of feeding products BAS: up to $5.1 \cdot 10^8$ CFU / g, which is 18.9 times higher than 15 days of age, as compared with the control - 16.5 time.

In the 4th group of pigs this ratio has increased over the 50 days of the experiment 1.7 times

Enterococcus population level for the entire period of experiment was 1,5-5,3 times higher than in the beginning of the experiment, except for the control group, which decreased to 1.2 times the lowest value for the number of weaned at the age of enterococci ($5 \cdot 10^4$ CFU / g).

The greatest increase in the number of yeasts and molds, characterized by a control group - 6.9 times. In other groups of microorganisms growing piglets data does not exceed 1.6 times (Group 4).

The results of the study of the large intestine contents of pigs department for quantitative content №100 strain show that in 45 days of age the number of cells of the strain, there were 2 times less than in piglets aged 60 days.

The dose received by a pig of the drug containing the strain №100, increased during this period by 1.2 times and the number of cells in the intestinal contents - in 2 times, indicating that the engraftment of this culture in the intestines of pigs.

When studying mutual antagonistic activity of strains of the genus Flavobacterium and №100 L.amylovorus BT 24/88 is not revealed suppressed-guide effect of these microorganisms with respect to each other in a dilution of $1:10^1$ - $1:10^4$ cfu / ml. The presence of DHQ-2 in the concentrations of 1 and 10 mg / ml did not inhibit the growth of microorganisms and do not change their tolerance towards each other.

Feeding tokokarina at a dose of 200-600 million. Cells per 1 head per day with DHQ-2 the rate of 10 mg per kg of food leads to an increase -daily gain by 9.4% ($P < 0.001$), while reducing feed consumption by 8.3% reduced morbidity 2 times for 50 days of the experiment - 35% between the ages of 10 to 45 days and 67.2% at the age of 45 to 60 days. The economic effect is increased by 7.9%.

Application lactoamilovorin at a dose of 8-10 ml per head per day in combination with DHQ-2 increases average daily gain by 6.7% ($P < 0.01$), while reducing feed costs by 6.1%, a decrease coli-operation with

diarrheal disease syndrome 2 weeks feeding drugs by 79.6% (for the entire period experienced an average of 33.6%) and increase the economic effect of 3.1%.

Joint application of probiotics and tokokarina lactoamilovorin combined with DHQ-2 promoted daily gain contributes to an increase of 21.5% ($P < 0.001$), while reducing feed consumption per 1 kg of a gain of 17.7%, reducing the number of disorders digestive system in the first month experiences by 19.3%, of pigs aged from 45 to 60 days at 79.1%, and for the entire test period by an average of 45.6%. The economic impact at the same time increased by 16.5%.

Using DHQ -2 in the diets of piglets increases the average daily gain of 15.9% ($P < 0.001$), while reducing the feed rate of 13.5%, reduce the incidence of 2 times. The economic effect is increased by 13.8%.

Application DGQ -2 in various combinations with probiotics and tokokarinom lactoamilovorin or without recovery of the intestinal probiotics promoted microbiocenosis. The highest-stabilized effect on the microbiological indicators of intestinal contents had application Ekostimul-2 in combination with tokokarinom and lactoamilovorin.

■ Investigations carried out on an experimental pig farm of the institute there were three groups of pigs of large white breed with 10 heads each, which were fed with complete feed SC-3, 4, 5 and 6, depending on the growing and fattening period. One group of pigs was also given with the DHQ-1, the other with arabinogalactan (AG) in doses of 1 mg and 75 mg per kilogram of body weight per day, respectively. Pigs were kept in standard housing with a ventilation system.

That year in July and August in the Moscow region 44 days with temperatures above 30° C, were registered, 33 of them in a succession. On 15 days the temperature exceeded 35° C, including 8 days continuously. In late July there was smog because of fires. This state of the environment affected the microclimate of the pig farm, where the air temperature was also higher than 30° C, with high concentration of smog. During this period, the pigs were on fattening at the age of 120-150 days.

Study morpho hematological indicators of pigs blood indicates that in piglets treated with feed additives in the suckling and postweaning growing, blood leukocytes content was significantly lower and amounted to in relation to the control of 68.4 and 64.6% respectively when giving DHQ-2 and AG. While the content of erythrocytes and hematocrit was higher by 4.8, 7.5 and 2.4%, 3.1%, respectively, a positive sign of the state of health. In the following 60 days growth, these figures leveled off with some advantage in piglets fed with DHQ-2. With the onset of heat and smog clinical condition of the piglets treated with food additives was better, especially in the group receiving AG having prebiotic and immunomodulatory properties.

Analysis of clinical screening tests of serum shows that the total content of protein in the control group piglets increased with age from 58.7 ± 2.86 at the age of 53 days to 68.25 ± 1.79 g / l to 194 days of age. This increase was due to globulin fraction, which increased during the period from 26.7 ± 1.94 to 38.30 ± 1.08 g / l while albumin decreased from 31.9 ± 0.93 to 29.95 ± 0.73 , indicating the reduction of albumin production hepatic function and the use of it as a backup protein for metabolism, generation of humoral immunity in connection with the effect of stressful environmental factors, one of which is the heat and smog.

The intensity of metabolic processes in the body of the control group of pigs is also evidenced by the elevated levels of serum urea and glucose, which may also indicate the inclusion of gluconeogenesis in the mechanism of homeostasis.

Effect on the organism of DHQ-2 and arabinogalactan was ambiguous because of their biological properties. For instance, giving AG to piglets during the period from 15 to 120 days of age stimulated both liver albumin production function and formation of the globulin fraction containing immunoglobulins, since one of the properties of AG is immunomodulating ability. However, under the stress because of heat and smog the total protein content in serum decreased in both fractions on the background of a lower level of urea and glucose in comparison to both the control group and the group receiving DHQ-2, which may indicate a more successful piglets organism protection as compared to the control group.

Effect on the pigs organism of DHQ-2 is manifested through its antioxidant and capillary protective properties, thereby providing increased activity and protection of cells of all organs and tissues of the body.

Effect of DHQ-2 on the biochemical parameters of blood serum was manifested mainly in postweaning and fattening period, which coincided with the period of heat and smog. During this period, these indicators characterized the best adaptive capacity of the organism as compared to both the initial state of this group of piglets, and to the control group and the one treated with AG.

Influence of technological and environmental stressors on the body of animals usually cause in it free-radical oxidation of lipids, which results in the rupture of membranes and the reduction of viability of cells in the body.

The use of the feed additives in the diet of pigs has blocked the process of lipid peroxidation during the entire period of growing and fattening, especially during the period of heat and smog. Thus, acid, peroxide value and malondialdehyde content in the blood serum of the experimental groups of pigs was lower than the control one by 17.6-31.2, 9.0-30.3 and 16.4-41.8%, respectively, and the body's antioxidant defense was higher, which was reflected in the increase in antioxidant activity of blood plasma, amounting to $1.32-1.55 \text{ L} \cdot \text{min}^{-1} \cdot 10^3$ in piglets of the experimental groups versus $1.25-1.37 \text{ L} \cdot \text{min}^{-1} \cdot 10^3$ in the control one.

The most effective feed additive was DHQ-2.

Homeostasis organism largely depends on the functional state of the liver. In the control group of piglets bilirubin content was above physiological norm and increased with age from 5.35 ± 1.27 to $13.94 \pm 3.10 \text{ uM} / \text{L}$, while in the experimental groups of piglets it also increased with age, but was significantly lower than that, which indicates positive hepatoprotective effect of the feed additives.

Activity level of aminotransferase - ALT and AST also characterizes the functional condition of the liver.

Serum AST is a microsomal fraction, whose share of the total activity of the enzyme is 60%. Increased AST activity is typical in the disorder of the cardiovascular system. ALT is a specific marker of hepatic function, activity of which is serum microsomal fraction. Increase in the activity of the enzyme is associated with hepatitis of different etiology.

All data morpho hematological and biochemical indices of piglets corresponded well to the intensity of growth in the various technological phases and periods of extreme positive temperature and smog.

Thus, the average daily gain of the piglets in the control group during the suckling period of growth was 227 g, post weaning - 456 g and the fattening period - 445 g, the latter coinciding with the effect of environmental stress.

Piglets treated with AG showed higher average daily than that in the control group by 5.7, 15.8 and 19.3% and the pigs fed with DHQ-2 - 18.9, 9.6 and 27.4% respectively, which is primarily due to its antioxidant properties.

■ When using DHQ-2 live weight broiler chickens increases with age is not the same. In the experimental group, the figure for the entire study period increased by 55.91 times and in control - at 52.18 times.

During the pilot period, broilers receiving DHQ-2 by live weight is not always superior to the control group counterparts. At the age of 7, 21 and 28 days of live weight poultry experimental group inferior counterparts in the control group 1,34-2,77%, while in the remaining age groups - superior - to 0,06-8,13%. By the end of the test period rate of broilers studied that received additive was 169.07 grams more than the control.

Absolute average weight gain in the experimental group increased with age. During the first, third and fourth week of the average daily weight gain of broilers fed DHQ-2, inferior to that of the control group chickens 3,50-4,71%, which corresponded to 0,44-2,94 g, and in other age groups - superior to 4,66-32,42% or 1,15-24,02 g, with a maximum observed superiority of the age of 42 days (Fig. 3.4).

The average weight gain during the study period (42 days) increased with each subsequent week in both groups, reaching a six-week age level of 53.86 g in the group treated DHQ-2, and 49.75 g in the control group. However, not always the value of the experimental group was greater than in the control. So, by the end of the first, third and fourth week of life, the absolute average daily gain of live weight of broilers of the experimental group was inferior to that of the representatives of the control group 1,51-3,50% in other age segments - excelled at 0,04-8,27% (0 , 02-4,11 g), and the maximum difference observed at the age of 42 days.

Thus, the analysis of dynamics of body weight showed that the application of DHQ in the dose of 1 mg / kg daily gain helped getting in broiler chickens for fattening period at the level of 53.86 g, which is 8.27% more than in growing broilers without feed additive. Protection of chickens of experimental group was 93%, while the control group - 85%.

Mass eviscerated carcasses examined chickens increases with age groups . In the experimental group the study to measure the age of slaughter became more in 131.8 times, and in the control group - to 110.1 times, respectively. In the period from 14 to 21 days of life of the mass of carcasses of chickens experimental group yielded test values of 1,30-5,30%. At the age of 7 days and 28 until the end of experiment, the rate in the group of chickens receiving DGQ 2 , superior to those of the control group at 2,97-19,71%, by the end of the test period the superiority of the experimental group of broilers of Test increased and reached 255.67 g .

Weight of meat in the carcasses broilers of the experimental group in most age groups exceeded that reference, in different ages ahead of the first control group of broilers by weight of meat on 0,33-24,34%. Only at the age of 14 days studied index in the experimental group was 0.29% below the reference level. By the 42-day-old broiler carcass test group reached a maximum advantage over those of the control in their content of meat an average of 211.36 g

The content of the bones in the carcasses broilers increases with age. In the control group of bone mass during the test period was more at 41.18 times, and in the group treated with DHQ-2 in 52.92 times. By the end of the first week in the period from 21 to 28 days broilers test group yielded analogs for control of bone mass in carcasses 5,46-16,69%, while in the remaining age groups - superior to 11,0-28,51%. By the 42-day-old broiler carcasses in the experimental group were bones at 59.40 g higher than in the control group.

Thus, the use of DHQ-2 contributed to weight gain gutted carcasses of broilers is primarily due to a more intensive growth of muscle mass.

The dry matter content in the meat of chickens treated with DHQ-2 varies with age from 22.75% to 28.99%. At the age of seven days in the analyzed experimental group rate control values inferior to 5.60%, at age 14 days - 1.85%, and in 28 days - 4.33%, in other age groups studied dry matter in the experimental group exceeded poultry meat control on 0,23-7,81%.

Changes in fat content in the meat of chickens experimental group demonstrated with age undulating character. At the age of seven days the analyzed index in the experimental group yielded analogs control 8.85%. The maximum concentration of fat in the meat of broilers experimental group was observed at 14 days, whereas the control group - 35 days. However, by 42 days of age, the fat content in the meat of poultry treated DHQ-2 was at 67.23% more than the control group in broilers.

The protein content in the meat of broiler chickens varies with age. In broiler control group changes in the composition of the protein fraction of the dry matter of meat were wavy character. In different age groups, the amount of protein in the control group averaged 16,45-21,78%. In broilers fed DHQ-2 , the proportion of protein in meat increased with age from 16.69% to 20.12%. In the period from 7 to 21 days analyzed index in the experimental group increased 1.15 times in the next two weeks, there was a slight decline in the proportion of protein. During the last week of the investigated period, the amount of protein in meat poultry experimental group increased by 1.13 times. By the 42-day-old broilers were superior to the control group experienced representatives of the absolute protein content in meat by 3.03%.

According to the content of total protein in blood serum of chickens treated DHQ-2, in most of the investigated age group outnumbered counterparts who received basic diet for 8,77-38,42%. Only at the age of 7 and 21 days in the test group broilers total protein inferior control values 11.70 and 12.26%, respectively. In the experimental group the minimum values of the studied index registered in the age of 21 days, and then with each subsequent week there was an increase of total protein concentration of up to 42-day age. In the control group of broilers mentioned period was characterized by alternating growth and decline in the total protein content in the blood serum.

Determination of the relative content of protein fractions of blood serum showed that the proportion of albumin in broilers of the experimental group in the majority of the studied ages inferior to the reference values from 0.02% to 9.05%. The proportion of α -globulin in the composition of total protein is also a control group of chickens was often above the rate of broilers fed DHQ-2. The overall dynamics of age changes the proportion of α -globulins in the experimental group was similar to that of the control group. The proportion of β - and γ -globulins are often exceeded in chickens of experimental group. Note that the β -globulin fraction of the bird in test group from 21- to 42-day-old, along with the increase of serum total protein content of the blood increases.

Analysis of the absolute content of protein fractions showed that during the period of most rapid growth of chicks observed a higher content of albumin fraction of serum proteins in poultry experimental group. Obviously, the albumin fraction, being the most finely divided, easily mobilized for the synthesis of the growing organism tissue proteins chickens. The content of albumin in the blood characterizes the level of protein metabolism in the body at all. In our experience, the highest content of albumin fraction was observed in birds receiving DHQ-2, at the age of 14 days. In the period from 28 to 42 days in the blood test group chickens albumin concentration exceeded the reference values at 7,72-30,64%.

Blood concentration of total bilirubin chickens of experimental group increased to three weeks of age, reaching a level of 6.90 mmol / l, after which there was a decrease of up to 42-day-old, sinking to the level of 2.0 mmol / l. At the same time during the first four weeks of the investigated parameters in broilers of the experimental group exceeded benchmarks for 16,67-305,90%, and in the last two weeks of the observed period - inferior 40,0-41,18%.

When studying the state of the enzymes found in chickens that ALT activity in blood day old birds averaged 9.20 U / l. During the first three weeks of life, this figure was reduced in both groups, but more intensively in broilers in the control group. As a result, the enzyme activity in the blood of chicks receiving DHQ-2 to 21-days age to reference values exceeded 79.59%. However, the increase in alanine aminotransferase activity in blood of broilers in the control group after three-week age, led to the fact that according to this indicator, the experimental group a bird in the last two weeks of the investigated period inferior to the control 41,01-70,51%.

AST activity in the blood test group only chickens aged three weeks was 1.43% higher than the control, but in other age groups, this figure for the test group broilers 11,51-29,99% was less than control values.

The activity of gamma glutamyl transferase, as a rule, increases in hepatic dysfunction and cardiovascular disease that occurs when toxic lesions.

Our findings γ -glutamyl transferase activity in blood broiler control group indicate that the rate of the control group birds age ranged between 176.10 nmol / l to $c^* 608.50$ nmol / l c^* , while in the test group - from 357.20 nmol / s $^* 1$ to 475.50 nmol / l with * .

The general trend of the changes in blood glucose concentrations chickens experimental group is similar to that of the control group birds.

Our research has shown that during the first two weeks of blood glucose broilers receiving DHQ-2 inferior test values 13,08-30,81%, and in the subsequent age periods - superior to 3,54-37,50%. By the 42-day age differences on the concentration of glucose in the examined groups did not exceed 1.0%.

LDH activity with age is subject to significant changes. At day-old chicks of the enzyme activity was on average 895.4 U / L. Note that if the birds in the control group blood lactate dehydrogenase activity ranged from 30.6 units / L to 3125.5 U / l, the test group broilers - from 79.1 units / L to 1987.0 U / l.

In the age of 28 and 42 days in the blood component examined test group broilers control values inferior to 75,1-78,6%, and in other age groups - was superior to 21,92-158,50%.

The activity of α -amylase in the blood of broilers tested groups was maximum at day old and averaged 58.90 mg / c*1 . This indicator chickens experimental group only at the age of seven days yielded control values 25.72% and in the rest of the studied age groups - superior to 13,17-355,6%. Changing the α -amylase activity in blood of the control group chicks ranged in age between 6.75 mg / c*1 to 52,10 mg/c*1 ,, and the bird experimental group - from 15.90 mg / c*1 to 45.15 mg / c*1...

Determination of cholesterol concentration showed that it was the content of day-old chicks in the blood of an average of $10,44 \pm 1,015$ mmol / l. In the blood of broilers in the control group was the amount of cholesterol in different age periods 2,52-4,51 mmol / l, and the birds of receiving DHQ-2 - 3,07-3,99 mmol / l. In the age of three and five weeks studied index in the test group was 7,96-21,29% lower than in the control, and in other age groups - 3,35-58,13% to above.

Age dynamics of the content of triglycerides in the blood of chickens control and experimental groups showed a different trend. Peaks triglyceride levels in the control group of chicks aged marked 7 and 21 days, and were at the level of 0.78 mmol / l. In broilers fed DHQ-2 maximum figure was examined at the age of 7 days and averaged 0.88 mmol / l, in other age groups, the number of the experimental group in the blood triglyceride bird was 0,34-0,54 mmol / l. At the age of 21 and 42 days of triglycerides in the blood test group broilers inferior to that of the control 56.13% and 12.99%, respectively, in other age groups, it was equal to or 12,82-74,19% compared with control.

3.4. The effectiveness of using DHQ-2 in beekeeping

DHQ-2 promoted reproduction of queen bee, normalized physiological status of bees in the period of early spring rehabilitation, increased physical endurance and vitality of bees, raised honey yield.

The high effectiveness of using DHQ-2 was achieved with its concentration of 3-5 mg /L in the saccharose solution poured into the drinker. As a result in two months, before main honey yielding in the control bees the queen bee laid daily on average 1202 eggs, while that in the experimental group was 1429 eggs, or 16,0% more. Honey yielding correlated with the reproduction gain of the bee family.

3.4.1. The study of DHQ-2 used against pathogenic microorganisms as alternative to antibiotics

Antimicrobial effect of different antibiotics and DHQ-2 to pathogenic, opportunistic, and probiotic microorganism was compared in vitro. In gel diffusion test with a series of dilutions the inhibition zone diameters were measured. The tested cultures of *Staphylococcus epidermidis* strain 14990, *Micrococcus luteus (lysodeicticus)* ATCC 4698, *M. luteus* ATCC 10240, *Escherichia coli* VL-613, *Pseudomonas aeruginosa* strain 98, *St. epidermidis* and *Ps. aeruginosa* were found to be high sensitive to 2.0 % and 5.0 % DHQ-2 but low sensitive to all the tested concentrations of bacitracin and 3 to 16 μ g per milliliter of grisin. Probiotic *E. coli* and nonpathogenic *M. luteus* ATCC 4698 and *M. luteus* ATCC 10240 of the gastrointestinal microflora seem to be insensitive to al the tested concentrations of DHQ-2 but high sensitive to the tested antimicrobial drugs.

CONCLUSION

The investigation of biological properties and effectiveness using of dihydroquercetin in husbandry, poultry and beekeeping was showed its positive influence on biocorrection metabolic health, productivity, reproduction and safety animals, beards and bees. It also showed its affinity to microorganisms in digestive tract and intensify effects when its used together with probiotics and other preparations. Dihydroquercetin can be in same cases a concurrent to antibiotics.

REFERENCES

1. Artemyeva O.A., Pereselkova D.A., Fomichev U.P. Dihydroergocristin, the bioactive substance, to be used against pathogenic microorganisms as an alternative to antibiotics. // Sel'skokhozyastvennaya biologiya [Agricultural Biology], -2015, V. 50, '4, p. 513-514/
2. Donnik I.M., Smirnov P.N. *Ecologiyay and zdjrovye jivotnyx*. Ekateriburg, UTK, 2001, -332 p.
3. Bloun P., De Poo D. Zdjrovye I vosproizvoditelnaay funkciay jivotnyx // Veterinariy sel'skochozystvennyh jivotnyh. – 2009. No 1, -S. 28-29.
4. Bollwein H. Declining fertility due to high yield ? //EuroFier innovaiton , 2010, -Netherlands, P.20-22/
5. Chen M. Report.The evolving threath of antimicrobial resistance. Options for action (<http://www.who.int/drugresistance/documents/surveillaencereport>)
6. Chernycha I.M., Tatulov U.V., Mittelschtein T., Susy I.V., Sovremennye trebovaniy k sbinine, postupayshey na promyschlennuy pererabotku. Svinovodstvo, -2009, No7, S.-4-8.
7. Koelemann E., Optimal liver support for healthy cow during transition. //All About Feeds.-2011, vol.2, No.2,-P.14-15/
8. Overton T.R., Waldron M.R., Nutritinal management of transition dairy cows; strageggies to optimize metabolic health //J.Dairy Sci. -2004, -Vol. 87, E.suppl.-P.-103-119/
9. Plotnikov M.B., Tuykavkina N.A., Plotnikova T.M., Lekarstvennye preparaty na osnove dikvertina. Tomsk, 2005, -228 p.
10. Suryasathaporn W., Heuer C., Noordhuizen-Stassen E.N., Schukken Y.H. Hyperketonemia and the impairment of udder defens: A review// Vet. Res. 2000. – Vol. 31, -P. 397-412.