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PHYSIOLOGICAL AND BIOCHEMICAL EFFECTS OF TWO FEED ANTIOXIDANTS IN MODELING TECHNOLOGICAL STRESS IN PIGS (*Sus scrofa domesticus* Erxleben, 1777)

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Abstract

Intensive livestock technologies do not fit well with the physiology of domestic species and put farm animals at risk of various health problems and disorders, which most negatively affects highly productive animals with intensive metabolism. Feed antioxidants might be a solution to improve productive health, adaptive capabilities and stress resistance of livestock. The outcome of adaptogen application depends on thorough elucidation of mechanisms of their action on physiological and biochemical processes in the body compromised by stress. Our study imitated social stress (modeled stress, MS) as the most common in intensive livestock to compare two dietary antioxidant additives of different origin and chemical composition. Thirty-six hybrid boars F_2 (Large White × Landrace) × Duroc aged 103 days (35 kg live weight) were assigned for four treatments (9 animals per each): 1 — control without MS, 2 — control with MS, 3 — MS + proteinate Se (PSe) (B-TRAXIM Selenium-11, PANCOSMA CANADA, Inc.; 0.2 mg a.i. per 1 kg feed), and 4 — MS + dihydroquercetin (DHQ) Ekostimul-2 drug (OOO Ametic, Russia; 32 mg a.i. per 1 kg feed). To simulate social stress, boars were moved every 14 days within the group to change the neighbors. Blood for assay was sampled three times over the trial from five boars of each group. With age, the blood cortisol level was revealed first to decrease by 36.8. 22.5, 41.3 and 52.8 % from the initial values in groups 1, 2, 3 and 4, respectively, though by the end of the final feeding there was a 46.4; 37.4; 8.1 and 60.4 % increase in the parameter. The cortisol concentration was the highest in group 3 (MS + PSe) during intensive growth (282 nmol/l vs. 211 and 214 nmol/l for groups 1 and 2). In groups 1, 2 (MS), and 3 (MS + PSe), the cortisol concentration reached 309, 294 and 305 nmol/l by the end of feeding. Blood cortisol level was the lowest in group 4 (+ DHQ), 134 nmol/l ($p = 0.07$ compared to group 2) at intensive growth and 215 nmol/l at final fattening, corresponding with thiobarbituric acid reactive substances (TBARS) levels which were also 6.7 and 12.3 % lower, respectively. Lactate dehydrogenase (LDH) activity and creatine phosphokinase (CPK) activity also altered. In group 1, LDH activity decreased from 459.4 to 377.5 IU/l over the trial. The same pattern was characteristic of group 4 (MS + DHQ). In group 2 (MS) and group 3 (MS + PSe), LDH activity declined to 317.0 and 289.3 IU/l by the end of feeding, which was 16.0 ($p < 0.01$) and 23.4 % ($p < 0.01$) less than in group 1. In group 4, the index, being constantly decreasing over the trial as in group 1, remained 15.0, 7.0 ($p = 0.06$ compared to control group 2 with MS) and 2.7 % lower than in groups 1, 2 and 3. The MS lowered the blood glucose concentration by 13.8 % ($p < 0.05$) compared to control 1 during the final fattening period. In group 3, this indicator as influenced by MS was also 7.4 % lower ($p < 0.05$), but due to PSe, a 7.4 % increase occurred compared to control group 2. Dietary DHQ led to the leveling of negative effects of MS, which, together with low cortisol indices in this group, stabilized the blood glucose concentration at the control level without MS in group 1. The DHQ was found to also contribute to a 25 % ($p < 0.01$) increase in blood triglycerides during final fattening compared to group 1 without stress. Pigs also differed in pathogenetic resistance. MS mobilized the cellular immunity through an increase in phagocytic activity PA ($p < 0.05$), phagocytic index PI ($p < 0.001$), and phagocytic number PN ($p < 0.05$) in control group 2 at the end of the test. PSe and DHQ normalized these indicators compared to control

(group 2) practically to the control values without MS ($p < 0.01$ for PI; $p < 0.01$ and $p < 0.05$ for PN, respectively). Thus, in animals fed adaptogens, the resistance indices at the end of the experiment corresponded to those in the control group 1, which indicates higher stress resistance, and DHQ additionally promoted humoral immunity as compared to the control group 1 ($p < 0.05$), which confirms the ability the adaptogens to enhance the body resistance to stress. Interestingly, despite the absence of statistically significant differences between most of the studied biochemical parameters ($p > 0.05$) which indicate a balanced animal diet, changes were noted that characterize the effect of the adaptogens under MS. In groups 2-4, blood phosphorus concentration was higher than in control group 1, 4.42 ($p = 0.07$), 4.52 ($p = 0.1$) and 4.64 mmol/l ($p < 0.05$) vs. 3.94 mmol/l. Thereof, the Ca/P ratio changed significantly during fattening. In group 2 (MS), group 3 (MS + PSe) and group 4 (MS + DHQ), the values 1.01 ($p < 0.05$), 0.99 ($p < 0.05$) and 0.89 ($p < 0.001$) vs. 1.15 in group 1 without stress. Blood morphology in pigs also changed as influenced by MS and the adaptogens. The counts of blood leukocytes in groups 2, 3 and 4 was 12.5; 5.4 and 6.1 % higher than in group 1 in the middle of fattening period, and 32.5 ($p < 0.05$), 40.1 ($p < 0.05$) and 21.7 % ($p = 0.07$) higher at the final fattening. A decrease in the number of erythrocytes and an increase in the hemoglobin amount in blood were characteristic of all groups. In general, by the end of feeding animals subjected to MS these two indicators were 6.6, 14.3, 9.7 % and 1.09, 6.09, 4.27 % higher than in group 1. An increase in blood erythrocytes ($p < 0.05$), hemoglobin ($p < 0.05$) and hematocrit ($p < 0.01$) in animals fed selenium vs. control group 2 indicates a decisive role of Se adaptogen as antioxidant during fattening. The observed changes were associated both with the action of cortisol generated by physiological stress, and with an increase in nonspecific resistance of boars due to the adaptogens. Importantly, the average daily weight gain in boars was close to that genetically conditioned for the genotype F_2 (Large White × Landrace) × Duroc. As a result, over the entire period of the trial, groups 1, 2, 3, and 4 showed an average increase of 1047, 1035, 1003 and 1042 g, respectively, of which the weight gain was the greatest in control 1 (without stress) and in group 4 fed DHQ at MS. Thus, our findings give grounds for further studying effects of these feed adaptogens for their proper use in intensive industrial pig breeding.

Keywords: stress, pigs, adaptogens, antioxidants, dihydroquercetin, selenium, cortisol, lactate dehydrogenase, hematological indicators, creatine phosphokinase, TBA-active products, nonspecific resistance

Intensive rearing of livestock commonly used nowadays antagonize the evolutionary physiology of farm animals [1]. The current priorities of animal breeding are genetically determined high productivity performance. However, the realization of such productive potential imposes extra physiological loads on an animal, aggravates effects of stress factors and significantly affects homeostasis that worsens quality of final products [2].

Stress triggers a cascade of non-specific adaptive (normal) responses of the body to the effects of various unfavorable factors (stressors) violating homeostasis, which includes special state of the nervous system as a whole. Hans Sely (1907-1982) was the first to introduce the concept of stress as a non-specific response of the body to any change [3]. In animal husbandry, depending on the cause, stress is classified as social (technological), ecological, dietary, and immunological [4]. In particular, social (or technological) stress in pigs occurs when animals are kept in pens with unfamiliar neighbors, upon isolation, weaning, transportation, veterinary measures, etc. Sensitivity to social stress is always individual and is often associated with genetic factors, which has been confirmed in many research works [5]. Social stress can be acute (immediately after regrouping) or chronic, when animals are kept in group pens or in isolation, and after a repeated regrouping [6]. The frequency of social interactions and aggressive behavior of animals increase with increasing housing density [7, 8], and the growth rate is positively correlated with the area of the pen per animal [9]. It is also known that the response to social stress depends on gender, and it is higher in males than in females [10, 11]. The weaning and transfer to growing and finishing are critical periods in the technology of raising pigs. The deprivation of maternal presence and milk, transfer to a new house, regrouping, change of feed and service personnel cause technological stress in piglets, as a result, morbidity increases, and the growth rate slows down. This decreases natural resistance and of humoral immunity, allowing conditionally

pathogenic microflora to become active, which leads to indigestion or respiratory pathology [12]. With chronic exposure to various stressful situations, free radical oxidation is activated with the depletion of antioxidant defense. In the body, syndromes of stress maladjustment, ketosis, hepatodystophia appear, and autoimmune processes occur [13].

Dietary antioxidants ensure stabilization of the level of free radicals, reduce the impact of environmental stress factors and increase the adaptive capacity of the body [14]. Bioflavonoid dihydroquercetin and the essential trace element selenium are substances with antioxidant activity. Dihydroquercetin from Daurian larch (*Larix dahurica* Turez) has a wide range of biological properties. It regulates metabolic processes, positively influences functions of organs and body systems (in particular, the cardiovascular system), is involved in the protection of healthy cells of the body from pathological changes by neutralizing radical activity. Selenium also belongs to strong antioxidants, prevents cardiovascular diseases, has an immunomodulatory effect on cellular and humoral immunity. Se is found in many functionally active proteins, the selenoproteins which, in particular, include glutathione peroxidases and thyrodoxin reductases. In addition, it prevents alimentary muscular dystrophy in animals.

Recent years have seen a rapid rise in a renewed interest of plant raw materials, since many plants, including vegetables and spices, contain antioxidants [15, 16], in particular, flavonoids and phenolic components [17, 18]. Flavonoids are secondary plant metabolites with a spectrum of pharmacological and biological properties [19, 20]. Dihydroquercetin ($C_{15}H_{12}O_7$) (DHQ) is the dominant component of the bioflavonoid complex of Diquertin. Dietary dihydroquercetin blocked lipid peroxidation during pig growing and fattening [21]. Ecostimul-2 (Russia), a DHQ-based feed additive fed to piglets for post-weaning period (50 mg per head per day) significantly weakened the impact of environmental stress factors and increased animal adaptiveness ensuring average daily weight gain of 496 g after weaning, that is, 20.6% higher than in the control individuals [22]. DHQ as a dietary additive blocked free radical lipid oxidation, enhanced antioxidant defense and improved liver functions during growing and fattening. In another experiment, quercetin weakened oxidative stress and decreased intestinal inflammation, with the decrease in levels of blood endotoxin, reactive oxygen species (ROS) and malondialdehyde (MDA) in the intestine, and the increase in height of villi of the jejunum [23]. There is a report that series of new 3-monoacylated dihydroquercetin derivatives with enhanced antioxidant properties have been synthesized [24].

Therefore, better reproductive health and stress resistance are currently critical parts of pig commercial rearing. This requires more detail understanding mechanisms of the effect of alimentary antioxidants on the body's physiology and biochemistry.

This work presents a complex evaluation of metabolic, hormonal, antioxidant and immune status in pigs under simulation of one of the most common technological stresses, the social stress, upon correction with antioxidant drugs to compare their capability of leveling the impact of the stressor.

The investigation aimed to compare the physiological and biochemical parameters characterizing productive and adaptive status in pigs that received antioxidant drugs based on dihydroquercetin and selenium under model technological stress.

Materials and methods. Thirty six cross-breed boars (*Sus scrofa domesticus*) F_2 (Large White × Landrace) × Duroc (35 kg live weight, 103 day old) after the growing period were assigned for four treatments (9 animals per each): 1 — control without MS, 2 — control with MS, 3 — MS + proteinate Se (PSe) (B-TRAXIM Selenium-11, PANCOSMA CANADA, Inc.; 0.2 mg a.i. per 1 kg feed),

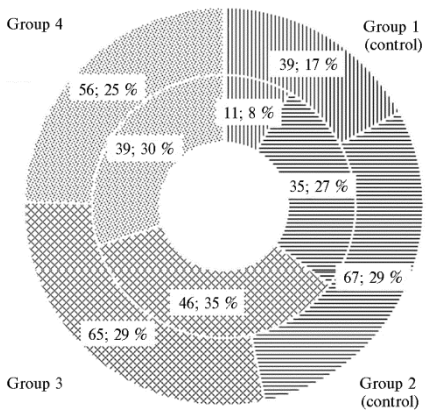
and 4 — MS + dihydroquercetin (DHQ) Ekostimul-2 drug (OOO Ametic, Russia; 32 mg a.i. per 1 kg feed). The basal diet (BD) included compound feeds SK-5 and SK-6 (Agrovitex LLC, Russia), balanced for nutrients and energy according to modern standards [25]. Doses of additives (as per active ingredients, a.i.) were 0.2 mg PSe and 32 mg DHQ per 1 kg feed according to the design of trials.

To simulate social stress, animals were moved from one pen to another within the group at the beginning of the experiment, and then every 14 days. After each relocation, animals were in the pen that were not previously neighbors.

Blood for assay was sampled from jugular vein of five boars of each group by puncture before the start of the experiment, before final fattening and before slaughter to analyze blood biochemical indicators (an automatic biochemical analyzer Chem Well (Awareness Technology, USA), morpho-hematological parameters (an ABC VET hematological analyzer, HORIBA ABX Diagnostics Inc., France), cortisol levels (by enzyme immunoassay), thiobarbituric acid reactive substances, TBARS (with a diagnostic kit, OOO Agat-Med, Russia), the total amount of water-soluble antioxidants (WA) (a device Tsvet-Yauza-01-AA, OAO NPO Khimavtomatika, Russia), activity of lactate dehydrogenase (LDH) and creatine phosphokinase (CPK) (a biochemical analyzer Bio Chem FC-360, HTI, USA). To assessed immune status, blood serum bactericidal activity (BSBA, a nonspecific resistance indicator) was assessed photonephelometrically, blood serum lysozyme activity (BSLA) by the Mutovin's method; phagocytic activity (PA) was assessed based on blood cell ingesting and digesting ability.

Obtained data were processed biometrically by the analysis of variance (ANOVA) method using STATISTICA 10 software (StatSoft, Inc., USA). The arithmetic means (M), the mean square error (±SEM) and the level of significance (p; differences were considered statistically significant at $p < 0.05$) were calculated. Comparison was performed with control group I (without MS) and group II (with MS).

Results. Social stress (overstrain associated with social adaptation to interaction in the community) very often occurs when raising pigs. In our tests, in animals of the control group I, which were kept without changing the pen, there were rare cases of aggressive behavior. MS in groups II (control), III and IV induced by animal relocation caused more restless and aggressive behavior. Animals from groups II, III and IV were more active when moving, often interacted with each other. The frequency of aggressive behavior directly depended on the percentage of restless animals in the group (Fig.).



Incidence of aggressive behavior (%) and the proportion of restless animals (%) in pigs (*Sus scrofa domesticus*) F2 (Large White × Landrace) × Duroc under modeling social stress. Outer circle corresponds to the number of cases of aggressive behavior (absolute value for the observation period and percentage of the total number of cases); inner circle is the number of restless animals (absolute value for the observation period and the percentage of the total number of cases) (experimental animal yard of Ernst Federal Science Center for Animal Husbandry, 2019, $N = 36$, $n = 9$).

The effect of MS was recorded by acts of aggressive behavior, which was especially clearly manifested in the first 2-3 days after relocation. Each time this period was characterized by the building of a hierarchical structure, a decrease in feed consumption, bites and increased injuries, anxiety, especially in groups II and III. So, aggressive behavior was least frequent in group 1 (39 cases) vs. 65, 67 and 56 cases (or 29, 29,

and 25% of their total number during the experiment) in groups 2, 3 and 4, respectively. In the group experienced MS, but fed dietary DHQ, the aggressive behavior diminished while anxiety was at the same level.

Importantly, the pig productivity (average daily weight gain) was close to genetically limited for the genotype F_2 (Large White × Landrace) × Duroc. As a result, over the experiment, there was an average increase of 1047, 1035, 1003 and 1042 g in groups 1, 2, 3 and 4, respectively, that is, it was greatest in control group 1 (without stress) and in group 4 (MS + DHQ).

We revealed significant differences in protein, nitrogen, carbohydrate, lipid and mineral metabolism in relationship with growth rate, MS and effects of dietary PSe and DHQ both between the groups of pigs and feeding periods. The blood levels of total protein and its fractions characterize the intensity and the type of protein metabolism and is closely related to growth, the influence of environmental factors and the diet [26]. In pigs of all groups, before fattening, the total blood protein ranged from 65.8 to 73.1 g/l, being within the physiological norm of 55-82 g/l. The same was observed for albumins (A) and globulins (G), 36.7-38.7 and 29.1-43.4 g/l, respectively, given a physiological norm of 19-43 and 26-57 g/l. The A/G ratio was higher than the average reference value, which indicated intense anabolism (Table 1). During the tests, the pattern of the change in total blood protein and its fractions in all groups was similar, that is, A/G ratio increased during intensive growth due to the albumin fraction and decreased by the end of fattening due to the globulin fraction. As a result, the A/G ratio increased over observation, which we consider positive. However, there were differences between the groups. So, in group 2 influenced by MS, the total protein level was 3.5% lower ($p < 0.05$) than in group 1 due to the albumin fraction and with an equal concentration of globulins, which could indicate the increased use of plastic substances for the energy needs of the body. During final fattening, the total blood protein in this group remained at the control level. The effect of adaptogens on protein metabolism was positive and differed depending on their biological activity. PSe and DHQ suppressed catabolism and enhanced anabolic processes during intensive growth of pigs experienced MS, as a result, total blood protein and its fractions remained the same as in the control group 1. At final fattening, the best characteristics of protein metabolism was in group 4 receiving DHQ. That is, the blood albumin level was 44.4 g/l at A/G = 1.78, with 41.9 g/l at A/G = 1.78, 44.4 g/l at A/G = 1.70, 42.4 g/l at A/G = 1.55, and 41.8 g/l at A/G = 1.64 for groups 1, 2 and 3, respectively, that is, the A/G value was the smallest in control group 2 under MS without correction (Table 1).

1. Metabolic parameters in pigs (*Sus scrofa domesticus*) F_2 (Large White × Landrace) × Duroc ($n = 5$, $M \pm$SEM, experimental animal yard of Ernst Federal Science Center for Animal Husbandry, 2019)

Parameter	Group			
	1 (control, BD)	modeling technological stress		
		2 (control, BD)	3 (BD + PSe)	4 (BD + DHQ)
Prior to growing (35 kg living weight)				
Total protein, g/l	65.82±1.29	70.28±6.23	73.19±6.43	71.73±2.95
Albumins (A), g/l	36.72±1.60	38.79±1.48	38.73±0.94	37.37±2.17
Globulins (G), g/l	29.10±0.74	34.49±6.22	43.47±6.98	34.37±3.71
A/G	1.27±0.08	1.36±0.22	1.24±0.18	1.15±0.19
Cholesterol, mmol/l	3.02±0.13	3.08±0.06	3.13±0.14	3.07±0.08
Phospholipids, mmol/l	0.30±0.05	0.36±0.08	0.35±0.05	0.35±0.12
Total bilirubin, μmol/l	4.46±1.30	5.64±1.03	3.03±0.69	5.07±0.70
AAT, IU/l	49.48±5.47	52.22±2.85	43.48±2.53	39.55±1.91
AST, IU/l	52.81±1.82	55.43±5.43	54.00±2.22	48.29±2.98
Prior to fattening (70 kg living weight)				
Total protein, g/l	78.36±0.59	75.64±1.12*	77.55±3.05	78.21±1.82
Albumins (A), g/l	47.04±0.73	44.06±1.20*	47.23±1.25	45.43±1.43

Continued Table 1

Globulins (G), g/l	31.32±0.55	31.58±1.98	30.32±2.46	32.79±1.98
A/G	1.50±0.05	1.42±0.13	1.59±0.12	1.40±0.11
Urea, mmol/l	5.73±0.47	5.88±0.58	8.59±1.25	6.81±1.07
Cholesterol, mmol/l	2.66±0.12	2.66±0.19	2.58±0.13	2.71±0.07
Phospholipids, mmol/l	0.46±0.10	0.44±0.14	0.55±0.53	0.56±0.13
AAT, IU/l	50.79±5.07	53.88±2.85	49.96±3.57	51.38±1.51
AST, IU/l	40.62±2.34	38.90±4.03	36.63±1.15	32.89±2.63*
Prior to slaughtering (100 kg living weight)				
Total protein, g/l	66.96±2.49	70.06±1.25	68.26±0.75	70.34±0.97
Albumins (A), g/l	41.98±1.46	42.44±1.58	41.83±2.68	44.44±1.63
Globulins (G), g/l	24.98±1.48	27.62±1.05	26.43±2.19	25.90±12.12
A/G	1.70±0.12	1.55±0.10	1.64±0.22	1.78±0.24
Urea, mmol/l	7.36±0.19	5.74±0.46**	6.64±0.56	6.73±0.86
Cholesterol, mmol/l	2.41±0.09	2.37±0.24	2.41±0.13	2.17±0.33
Phospholipids, mmol/l	0.69±0.13	0.75±0.16	0.64±0.16	0.59±0.20
AAT, IU/l	42.29±5.75	47.04±4.40	42.11±4.56	40.98±3.76
AST, IU/l	16.24±1.25	17.54±1.32	20.64±4.33	21.89±6.39

Note. BD — basal diet, AAT — alanine aminotransferase, AST — aspartat aminotransferase. For design of trials and description of treatments, see *Materials and methods*.

*, ** Differences between the treatment and the control group 1 are statistically significant at $p < 0.05$ and $p < 0.01$, respectively.

In the trials, the blood urea concentration in all groups corresponded to physiological limits (3.5-9.2 mmol/l). During intensive growth, its value in animals from control groups was the same. At final fattening, the blood urea increased in control group 1 (by 28.4%), but not in control group 2 (5.88 vs. 5.74 mmol/l, respectively). It should be emphasized that the urea concentration in the groups subjected to MS was lower than the control values without MS, and in the control group 2, we recorded its significant decrease ($p < 0.01$). Elevation of blood urea levels in a body with a normal urea cycle in the liver could be associated with a decrease in the intensity of protein renewal in tissues and anabolic processes. The effect of adaptogens we observed was as follows. The blood urea in pigs from group 3 (MS + PSe) and group 4 (MS + DHQ) was 49.9 and 18.8% higher, respectively, than in control 1 (without MS), and 46.0 and 15.5% higher, than in group 2 (MS). At final fattening, this indicator decreased by 22.8 and 1.2%, respectively, due to adaptogens, as a result, it equaled and amounted to 6.64 and 6.73 mmol/l, while in the control groups 1 and 2, the values were 7.36 and 5.74 mmol/l (see Table 1). We did not find statistically significant differences with group 2 (control with MS) when analyzing obtained data.

Lipids, namely cholesterol, phospholipids and triglycerides, as constitutive parts of cell membranes, are vital factors in the body life, especially under physiological stress. The blood cholesterol level in pigs of all groups was practically equal and fluctuated within 2.17-3.13 mmol l. Nevertheless, there was a regularity in its 10.1, 13.1, 13.1 and 29.4% decrease by the end of fatteningn for groups 1, 2, 3 and 4, respectively, but without statistically significant differences with the control groups, which indicates the stability of this parameter under MS. The blood phospholipids varied in the level within 0.30-0.75 mmol/l and increased by the end of fattening. Note that the phospholipids increased during intensive growth in groups with adaptogens (0.55 and 0.56 mmol/l, respectively, vs. 0.46 and 0.44 mmol l in groups 1 and 2). In contrast, by the end of fattening, the increase was more significant in the control groups (up to 0.69 and 0.75 mmol/l, respectively, vs. 0.64 and 0.59 mmol/l in the groups with adaptogens) (see Table 1). In general, analysis of blood lipids during the trials revealed the effect of MS on energy metabolism and its correction due to the adaptogens. Note that the DHQ was more effective.

The activity of blood ALT and AST in all groups during trials was within

physiological limits (for ALT and AST, 22-98 and 19-96 IU/l, respectively), varying within 39.55-53.88 and 16.2-55.43 IU/l, respectively. There was a slight increase in ALT activity during intensive growth with a decrease by the end of fattening. The change in AST activity was more significant and had a different character. A constant decrease occurred over the experiment, with 69.3, 68.3, 52.6 and 44.7% final decrease as per groups, respectively, which could indicate suppression of protein metabolism and the use of amino acids for energy purposes (see Table 1). DHQ smoothed the change in group 4 under MS, which was also expressed in a more noticeable ($p < 0.05$) decrease in values during the first period of growing, but at the end of the trials in the groups with adaptogens, this indicator was more stable, while in the control groups it was below the physiological norm

MS and the adaptogens used for its biocorrection influenced some of the processes of mineral metabolism. In phosphorus-calcium metabolism, phosphatases are essential which cleave ether bounds to remove the phosphoric acid residues from its organic ethers [27, 28]. Alkaline phosphatase is found in almost all body tissues [28]. In pigs of all groups, the activity of blood alkaline phosphatase varied within 222.0-516.1 IU/l at a physiological norm of 130-501 IU/l. Its highest and practically equal activity between the groups was observed in pigs receiving adaptogens, and the lowest in control 2. The observed characteristic pattern was a decrease in the enzyme activity by the end of fattening, which was approximately the same in all groups, by 48.4, 45.1, 42.4 and 50.2%, of the initial values) (Table 2).

2. Mineral metabolism in pigs (*Sus scrofa domesticus*) F_2 (Large White × Landrace) × Duroc ($n = 5$, $M \pm$SEM, experimental animal yard of Ernst Federal Science Center for Animal Husbandry, 2019)

Indicator	Group			
	1 (control, BD)	modeling technological stress		
		2 (control, BD)	3 (BD + PSe)	4 (BD + DHQ)
Prior to growing (35 kg living weight)				
Alkaline phosphatase, IU/l	447.35±64.31	403.93±26.35	446.27±11.27	516.11±80.53
Ca, mmol/l	3.36±0.13	3.28±0.09	3.32±0.16	3.45±0.45
P, mmol/l	3.03±0.21	3.20±0.20	3.02±0.12	2.99±0.23
Ca/P	1.46±0.12	1.35±0.11	1.43±0.09	1.52±0.12
Mg, mmol/l	1.68±0.06	1.63±0.04	1.66±0.03	1.65±0.09
Fe, mmol/l	25.27±0.86	21.51±2.55	24.02±2.23	22.23±2.06
Chlorides, mmol/l	96.04±1.58	95.51±3.24	94.97±2.30	95.89±3.12
Prior to fattening (70 kg living weight)				
Alkaline phosphatase, IU/l	406.90±17.70	389.77±11.86	446.27±11.27[b]	445.46±43.20
Ca, mmol/l	3.49±0.03	3.45±0.08	3.43±0.11	3.18±0.17
P, mmol/l	3.94±0.17	4.42±0.20	4.52±0.30	4.64±0.28*
Ca/P	1.15±0.04	1.01±0.03*	0.99±0.07*	0.89±0.04***[a]
Mg, mmol/l	0.99±0.03	1.16±0.07*	1.09±0.03*	1.17±0.11
Fe, μmol/l	25.10±1.74	28.49±1.92	31.38±3.58	25.91±1.54
Chlorides, mmol/l	119.22±3.35	117.47±2.62	119.39±1.82	119.32±7.64
Prior to slaughtering (100 kg living weight)				
Alkaline phosphatase, IU/l	230.95±31.73	222.06±29.27	257.38±37.69	255.09±23.90
Ca, mmol/l	2.96±0.06	2.95±0.09	2.91±0.08	2.93±0.03
P, mmol/l	3.06±0.16	3.09±0.19	3.11±0.18	3.26±0.14
Ca/P	1.26±0.07	1.26±0.10	1.23±0.09	1.17±0.05
Mg, mmol/l	0.84±0.03	0.81±0.02	0.85±0.05	0.86±0.06
Fe, μmol/l	25.27±1.60	28.55±0.81	24.92±2.81	28.38±2.72
Chlorides, mmol/l	111.38±2.60	109.21±2.34	106.03±1.64	105.87±2.84

Note. BD — basal diet. For design of trials and description of treatments, see *Materials and methods.*

*, **, *** Differences between the treatment and the control group 1 are statistically significant at $p < 0.05$, $p < 0.01$ and $p < 0.001$, respectively.

[a], [b] Differences between the treatment and the control group 2 are statistically significant at $p < 0.05$ and $p < 0.01$, respectively.

The blood calcium level in all groups was similar during the trials and varied over periods within 2.91-3.49 mmol/l, being within the physiological limits (2.0-3.6 mmol/l). Nevertheless, its amount slightly increased during intensive

growth (except for group 4) and decreased up to 2.91-2.96 mmol/l in all groups by the end of fattening. The P concentration changed in a similar way, did not exceed the physiological limits of 2.3-4.9 mmol/l, though depended on effects of MS and adaptogens. In blood phosphorus, there was a 17.2, 38.1, 49.6 and 55.1% increase during intensive growth, and a 22.4, 30.1, 31.2 and 29.8% decrease by the end of fattening compared to the period of intensive growth. As a result, the blood phosphorus concentration was practically equal between groups, 3.06, 3.09, 3.11 and 3.26 mmol/l (see Table 2). Changes in phosphorus levels significantly influenced the Ca/P ratio. During intensive growth, the Ca/P value decreased by 21.3 and 25.2% in the controls, and by 30.8 and 41.5% with adaptogens. By the end of fattening, the Ca/P value was almost equal in all groups, 1.26, 1.26, 1.23 and 1.17, respectively. We explain the variability of blood phosphorus at different stages of growing and fattening by its participation in energy metabolism. In particular, with MS during intensive growth in groups 2-4, the blood phosphorus concentration was higher than in control group 1, 4.42 ($p = 0.07$), 4.52 ($p = 0.1$) and 4.64 mmol/l ($p < 0.05$) vs. 3.94 mmol/l. In this regard, the Ca/P ratio in the middle of the growing and fattening periods changed significantly. In control group 2 and groups with PSe and DHQ, its value was lower, 1.01 ($p < 0.05$), 0.99 ($p < 0.05$) and 0.89 ($p < 0.001$) vs. 1.15 in the control group 1.

The physiological level of magnesium in pigs is 0.9-1.7 mmol/l. In our trials, blood magnesium did not differ between groups, decreasing during intensive growth towards the end of final fattening. At the beginning and end of the experiment, this indicator was within the reference values (see Table 2). In the groups with MS its values in the middle of the fattening period were higher than the control values ($p < 0.05$).

Blood Fe of 25.10-25.27 μmol/l was stable in the control group 1 throughout the trials. In the control group 2 under MS, it increased from 21.5 to 28.49 μmol/l during intensive growth, and remained unchanged until the end of fattening. In groups 3 and 4, blood Fe also increased during intensive growth, but then it decreased in group 3 to the initial value by the end of fattening, while continued to rise in group 4 (with DHQ) to the value in the control group 3; in groups 3 and 4, the Fe concentration was 28.5 and 28.4 μmol/l, respectively (see Table 2). Changes in blood chlorides throughout the trials were similar in all groups, with a 22.9-25.7% increase during intense growth and a 6.4-7.0% decrease by the end of fattening in the control groups and an 11.21-11.3% decrease in groups with adaptogens (see Table 2).

Cortisol is a stress hormone that protects the body from sudden fluctuations in physiological balance [29]. Cortisol enhances proteolysis, followed by synthesis of carbohydrates from protein breakdown products [30]. The body's antioxidant defense is designed to maintain the balance of BAC (biologically active compounds — lipids, peptides, vitamins, and other compounds) in the organs and tissues to protect from ROS [31].

The blood levels of cortisol, TBARS and water-soluble antioxidants (WA) did not significantly differ under the influence of MS and adaptogens over all periods. though there were some changes. In all groups, the blood cortisol level during intensive growth decreased with age by 36.8, 22.5, 41.3 and 52.8% from the initial values, and increased by 46.4, 37.4, 8.1 and 60.4%, respectively, at the end of fattening. The smallest values of 134 nmol/l ($p = 0.07$ vs. group 2) during intensive growth and of 215 nmol/l during final fattening were in group 4. The highest value was characteristic of the group with PSe during intensive growth, 282 nmol/l vs. 211 and 214 nmol/l in control groups 1 and 2. At the end of fattening in groups 1-3, the blood cortisol concentration became equal, 309, 294 and 305 nmol/l. Thus, before the final fattening, in stressed pigs fed DHQ the

blood cortisol level was minimal compared to other groups and 37.3 and 47.5% lower than in group 2 (MS) and group 3 (MS + PSe). This corresponds with TBARS levels which were also 6.7 and 12.3% lower, respectively (Table 3).

3. Blood cortisol concentration and antioxidant status in pigs (*Sus scrofa domesticus*) F_2 (Large White × Landrace) × Duroc (n = 5, M±SEM, experimental animal yard of Ernst Federal Science Center for Animal Husbandry, 2019)

Indicator	Group			
	1 (control, BD)	modeling technological stress		
		2 (control, BD)	3 (BD + PSe)	4 (BD + DHQ)
Prior to growing (35 kg living weight)				
Cortisol, nmol/l	334±116	276±54	480±48	284±73
TBARS, μmol/l	4.18±0.29	3.67±0.48	4.10±0.80	4.45±0.50
Total WA, mg/g	26.12±0.67	24.26±1.10	26.06±0.97	25.40±1.11
Prior to fattening (70 kg living weight)				
Cortisol, nmol/l	211±65	214±34	282±45	134±26
TBARS, μmol/l	3.08±0.21	3.14±0.14	3.34±0.45	2.93±0.54
Total WA, mg/g	12.20±0.64	11.28±0.88	12.20±0.90	11.76±1.00
Prior to slaughtering (100 kg living weight)				
Cortisol, nmol/l	309±107	294±111	305±61	215±53
TBARS, μmol/l	3.22±0.35	3.41±0.34	3.08±0.25	3.47±0.50
Total WA, mg/g	12.54±0.48	12.04±0.69	13.30±1.30	12.32±0.96

Note. BD — basal diet. TBARS — thiobarbituric acid reactive substances, WA — water-soluble antioxidants (total). For design of trials and description of treatments, see *Materials and methods.*

TBARS values [31] were in line with the level of total water-soluble blood antioxidants. These indices during the entire trial had similar values in all groups with a noticeable decrease under the action of MS during intensive growth and before slaughter, and an upward trend in pigs received adaptogens (see Table 3).

4. Activity of blood enzymes in pigs (*Sus scrofa domesticus*) F_2 (Large White × Landrace) × Duroc in a relationship with metabolism of carbohydrates and lipids (n = 5, M±SEM, experimental animal yard of Ernst Federal Science Center for Animal Husbandry, 2019)

Indicator	Group			
	1 (control, BD)	modeling technological stress		
		2 (control, BD)	3 (BD + PSe)	4 (BD + DHQ)
Prior to growing (35 kg living weight)				
Triglycerides, mmol/l	0.35±0.07	0.32±0.06	0.37±0.04	0.36±0.03
Glucose, mmol/l	9.17±1.27	8.47±0.45	7.07±0.69	6.49±0.50
LDH, IU/l	459.4±171.4	378.5±39.8	375.9±34.3	390.9±24.0
CPK, IU/l	2769.2±1698.6	1996.0±715.5	2656.5±856.5	2927.5±1315.2
Creatinine, μmol/l	76.3±5.7	92.5±13.0	82.6±9.0	86.4±11.3
Prior to fattening (70 kg living weight)				
Triglycerides, mmol/l	0.32±0.04	0.32±0.03	0.34±0.09	0.25±0.02[a]
Glucose, mmol/l	8.41±0.80	7.65±0.56	7.81±0.48	7.32±0.44
LDH, IU/l	407.5±22.4	450.9±28.4	423.9±25.1	379.2±24.3
CPK, IU/l	878.9±260.9	1649.5±779.4	1591.4±654.0	1018.7±429.2
Creatinine, μmol/l	124.2±8.8	108.2±6.8	122.0±10.9	122.0±8.3
Prior to slaughtering (100 kg living weight)				
Triglycerides, mmol/l	0.28±0.03	0.28±0.01	0.32±0.04	0.35±0.05**
Glucose, mmol/l	6.87±0.70	5.92±0.32*	6.36±0.56*	6.48±0.68
LDH, IU/l	377.5±44.3	317.0±23.8**	289.3±34.5**	367.4±33.6
CPK, IU/l	2484.0±916.6	1796.9±643.8	1368±573.5	3229.5±1261.6
Creatinine, μmol/l	112.9±11.9	101.4±9.1	103.4±4.5	107.8±10.7

Note. BD — basal diet. LDH — lactate dehydrogenase, CPK — creatine phosphokinase. For design of trials and description of treatments, see *Materials and methods.*

*, ** Differences between the treatment and the control group 1 are statistically significant at $p < 0.05$ and $p < 0.01$, respectively.

[a] Differences between the treatment and the control group 2 are statistically significant at $p < 0.05$.

Creatinine, a product of protein metabolism is formed in muscle tissue from creatine [32]. The blood creatinine level in pigs over the trials was within the physiological norm (78-148 μmol/l) with an increase during intensive growth and a decrease by the end of fattening. However, there were differences between the groups. During intensive growth, the creatinine level increased by 17.0% in the

control group 2 under MS, and by 62.8% in the control group 1. In groups 3 and 4 with adaptogens, the increase level was intermediate between groups 1 and 2, by 47.7 and 41.2%, respectively. As a result, in groups 1, 3 and 4 the indicator was 124.2, 122.0 and 122.0 vs. 108.2 μmol/l in group 2 (Table 4), which is associated, among other things, with the action of adaptogens under MS. Before slaughter, the creatinine pattern was the same with its lowest value in group 2.

Glucose metabolism at the cellular level largely depends on the hormonal status of the body. In particular, glucocorticoids (cortisol and others), promoting synthesis of carbohydrates from nitrogen-free amino acid residues, inhibit the oxidation of glucose, which leads to an increase in its blood level [30]. Thyroid hormones increase the absorption of glucose from the intestine, which also leads to its accumulation in the blood [33]. The hormones of the anterior lobe of the hypophysis, the somatotropin, corticotropin, and thyrotropin also exhibit a hyperglycemic effect [34]. In our trials, the blood concentration of glucose across groups and over periods ranged within 5.92-9.17 mmol/l. A pattern appeared in a decrease in this indicator by the end of the trials. Blood glucose was more stable in group 4 (+ DHQ). At final fattening, the adaptogens stabilized the blood glucose level. MS reduced the glucose concentration by 13.8% ($p < 0.05$) compared to the control without MS. In group 3, MS reduced this indicator by 7.4% ($p < 0.05$), but under the influence of PSe it increased compared to group 2 by the same 7.4%. Dietary DHQ allowed animals to escape negative effects of MS, which, given low cortisol indices in this group, stabilized the blood glucose concentration at the control level without MS (see Table 4).

Lactate dehydrogenase (LDH) is zinc-containing intracellular enzyme responsible for energy metabolism through the catalysis of lactic acid oxidation to pyruvate. LDH is found in almost all cells of the body and is most active in skeletal muscles, heart muscle, kidneys, liver, and erythrocytes [35]. Before the start of the trials, the blood LDH activity in pigs was 375.9- 390.9 IU l in groups 2-4, and 459.4 IU/l in the control group 1. Further, in group I, it constantly decreased, to 407.5 IU/l before final fattening and to 377.5 IU/l before slaughter. In groups 2 and 3, the activity of LDH under MS before the final fattening increased by 19.1 and 12.8%, then decreased to 317.0 and 289.3 IU/l, which was 16.0% ($p < 0.01$) and 23.4% ($p < 0.01$) less than in group 1. In group 4, this indicator steadily decreased over the trials, as in group 1, remaining 15.0, 7.0 ($p = 0.06$ vs. group 2) and 2.7% lower than in groups 1, 2 and 3, respectively (see Table 4). Blood LDH activity and its dynamics characterize physiological load on the body in the experiment and the effect of antioxidants on the energy metabolism in the muscles. It should be noted that due to DHQ, the LDH activity was the same as in animals that did not undergo MS, that is, it did not change significantly under the influence of a stress factor.

Creatine phosphate is a phosphagen that prevents the rapid depletion of ATP pool by supplying an easily usable macroergic phosphate required for ATP resynthesis from ADP. In the process of regeneration of ATP during muscle relaxation, creatine phosphate transfers a high-energy phosphate to ADP. The products of this reaction are ATP and creatine. Phosphorylation of creatine is catalyzed by creatine phosphokinase (CPK), an enzyme specific for muscles [36]. In all groups at the beginning of the trials, the CPK activity was within 1996-2927 IU/l. With intensive growth, the indicator decreased across groups by 78.3, 17.4, 40.1 and 65.3%. At the end of fattening (before slaughter), the CPK activity increased by 282.9, 8.9 and 316.9% in groups 1, 2 and 4, while decreased in group 3 by 14.1%. These results reflect the change in energy expenditure in the form of macroergs in different periods of the trials and the effect of antioxidants (see Table 4).

Blood triglycerides varied in all groups in range of 0.66-0.95 mmol/l and increased by the end of the final fattening. The smallest increase in concentration (by 27.1%) occurred in group 1, the largest (by 42.4%) in group 2. Under the effect of adaptogens, the increase was 30.1 and 30.9%, which was close to the indicators in group 1 (control without MS). The use of DHQ promoted a 25% increase ($p < 0.01$) in triglyceride amount as compared to the control group without stress.

5. Nonspecific immunity indicators in pigs (*Sus scrofa domesticus*) F_2 (Large White × Landrace) × Duroc in a relationship with metabolism of carbohydrates and lipids ($n = 5$, $M \pm$SEM, experimental animal yard of Ernst Federal Science Center for Animal Husbandry, 2019)

Indicator	Group			
	1 (control, BD)	modeling technological stress		
		2 (control, BD)	3 (BD + PSe)	4 (BD + DHQ)
Prior to growing (35 kg living weight)				
Lysis, %	41.16±1.29	40.40±0.85	40.41±1.53	40.68±2.00
Lysozyme:				
μg/ml blood serum	0.75±0.03	0.75±0.03	0.72±0.03	0.71±0.05
specific activity units (u/mg protein	3.36±0.18	3.21±0.04	3.15±0.15	3.08±0.13
BSBA, %	52.38±0.95	54.29±1.65	44.76±5.04	50.48±5.30
PA, %	40.33±1.86	39.0±2.31	43.33±2.60	49.67±4.67
PI	2.85±0.10	2.72±0.05	2.73±0.16	2.47±0.18
PN	1.15±0.03	1.06±0.08	1.19±0.13	1.23±0.17
Prior to slaughtering (100 kg living weight)				
Lysis, %	22.82±2.48	27.81±6.21	30.10±2.86	42.04±4.84*
Lysozyme:				
μg/ml blood serum	0.44±0.04	0.52±0.09	0.57±0.05	0.79±0.10*
specific activity units (u/mg protein	2.19±0.28	2.40±0.45	2.56±0.17	3.25±0.32
BSBA, %	52.69±1.08	52.69±1.08	54.84±1.86	52.69±2.15
PA, %	48.68±1.46	54.67±2.33	48.88±1.05	49.89±3.62
PI	2.36±0.04	2.92±0.04***	2.50±0.07[b]	2.38±0.07[b]
PN	1.15±0.05	1.60±0.08**	1.22±0.01[b]	1.19±0.12[a]

Note. BD — basal diet. BSBA — blood serum bactericidal activity, PA — phagocytic activity, PI — phagocytic index, PN — phagocytic number PN. For design of trials and description of treatments, see *Materials and methods.*
*, **, *** Differences between the treatment and the control group 1 are statistically significant at $p < 0,05$, $p < 0.01$ and $p < 0.001$, respectively.
[a], [b] Differences between the treatment and the control group 2 are statistically significant at $p < 0.05$ and $p < 0.01$, respectively.

Unfavorable environmental factors directly affect the pathogenetic resistance, involving bactericidal and lysozyme activity of blood serum and the phagocytic activity of the blood [37]. Before the start of the experiment, these indicators in all animals had similar values. Before slaughter, in the control groups, the BSLA value decreased and the phagocytic activity significantly increased with a relatively stable BSBA. In the groups receiving adaptogens, the indicators of resistance also changed, but differed significantly from those in groups 1 and 2. By the end of fattening in pigs receiving PSe, with a decrease in lysis and lysozyme concentration in the blood serum, there was an increase in BSBA (from 44.76 to 54.84%) and FA (from 43.3 to 48.3%), whereas in group 2 BSBA decreased (from 54.29 to 52.69%) and FA increased (from 39.0 to 54.6%). Dietary DHQ increased lysis from 40.68 to 42.04%, the lysozyme concentration from 0.71 to 0.79 μg/ml and BSBA from 50.48 to 52.69% with relatively stable FA values. These data indicated the mobilization of the body's resources when exposed to simulated stress. MS promoted mobilization of cellular immunity, expressed in an increase in phagocytic activity PA ($p < 0.05$), phagocytic index PI ($p < 0.001$), and phagocytic number PN ($p < 0.05$) in the control group 2 at the end of the trials. PSe and DHQ normalized these parameters as compared to the control group 2 practically to values without MS (PI at $p < 0.01$, PN at $p < 0.01$ and $p < 0.05$ in the first and the second case, respectively. Thus, in animals fed adaptogens, the resistance indices at the end

of the trials corresponded to those in the control group I, which additionally indicates an increase in resistance to stress (Table 5). DHQ additionally contributed to an increase in humoral immunity compared to group 1 ($p < 0.05$).

6. Morpho-hematological indicators in pigs (*Sus scrofa domesticus*) F_2 (Large White × Landrace) × Duroc in a relationship with metabolism of carbohydrates and lipids ($n = 5$, $M \pm$SEM, experimental animal yard of Ernst Federal Science Center for Animal Husbandry, 2019)

Indicator	Group			
	1 (control, BD)	modeling technological stress		
		2 (control, BD)	3 (BD + PSe)	4 (BD + DHQ)
Prior to growing (35 kg living weight)				
Leukocytes, $\times 10^9$/l	15.32±1.70	16.12±1.28	13.27±1.09	14.89±2.00
Erythrocytes, $\times 10^{12}$/l	11.30±0.17	11.07±0.37	11.58±0.70	11.05±0.32
Hemoglobin, g/l	130.96±2.86	127.00±3.00	126.44±6.52	131.10±3.58
Hematocrit, %	63.02±1.14	60.99±1.74	61.04±3.31	62.43±1.85
Color index, points	3.43	3.46	3.29	3.57
Prior to fattening (70 kg living weight)				
Leukocytes, $\times 10^9$/l	13.57±1.10	15.27±1.01	14.31±0.71	14.41±0.76
Erythrocytes, $\times 10^{12}$/l	10.51±0.23	10.57±0.31	11.29±0.05**[a]	10.55±0.32
Hemoglobin, g/l	133.13±3.05	130.06±5.79	136.12±2.72	135.78±4.50
Hematocrit, %	61.94±1.19	60.23±2.73	62.81±1.17	62.47±2.46
Color index, points	3.80	3.71	3.64	3.87
Prior to slaughtering (100 kg living weight)				
Leukocytes, $\times 10^9$/l	9.04±0.74	11.98±1.16*	12.67±1.45*	11.01±0.78
Erythrocytes, $\times 10^{12}$/l	9.02±0.69	9.62±0.29	10.31±0.15[a]	9.90±0.30
Hemoglobin, g/l	118.24±8.06	121.14±2.15	131.30±3.44[a]	106.98±26.7
Hematocrit, %	52.82±3.81	53.91±0.88	58.91±1.45[b]	57.09±1.89
Color index, points	3.94	3.78	3.82	3.24

Note. BD — basal diet. For design of trials and description of treatments, see *Materials and methods*.
*, ** Differences between the treatment and the control group 1 are statistically significant at $p < 0.05$ and $p < 0.01$, respectively.
[a], [b] Differences between the treatment and the control group 2 are statistically significant at $p < 0.05$ and $p < 0.01$, respectively.

Morpho-hematological traits showed characteristic differences between groups over trials, both in the values and dynamics. As compared to group 1, the number of leukocytes under MS in groups 2, 3 and 4 was 12.5, 5.4, 6.1% higher during intensive growth, and 32.5 ($p < 0.05$), 40.1 ($p < 0.05$), 21.7% ($p = 0.07$) higher at the final fattening. Their counts decreased in all groups except for group 3 where a slight increase occurred during intensive growth. The observed changes are caused both by the effect of cortisol under physiological stress and an increase in nonspecific resistance due to adaptogens (see Table 5). The level of erythrocytes, the hemoglobin and hematocrit values during intensive growth differed little. A decrease in the number of erythrocytes and an increase in the level of hemoglobin were characteristic of all groups of pigs. In general, by the end of fattening, these two indicators were 6.6, 14.3, 9.7%, and 1.09, 6.09, 4.27% higher, respectively, under MS than in group 1 (Table 6). Also note higher levels of erythrocytes ($p < 0.05$), hemoglobin ($p < 0.05$) and hematocrit ($p < 0.01$) in the group fed dietary selenium as compared to the control group 2 subjected to MS without adaptogens, which indicates a significant antioxidant role of Se in fattening.

Thus, the stress in the trials generated a long-term effect characteristic of distress. The leading factor was the struggle for leadership, which led to overexcitation of animals and, as a result, to injuries, loss of appetite, variation in periods of rest and feed intake, and to some changes in the physiological and biochemical status. The consequences of this type of stress can be observed up to 15-20 days after the onset [2, 9]. In our tests, regrouping occurred every 14 days, during which animals experienced all stages of stress response. However, it was more pronounced in the first 2-3 days after the regrouping. Physiological and biochemical parameters of pigs were assessed on day 42, that is, after 3-fold stress cycle, and

before slaughter on day 70 after two final cycles. It should be noted that regrouping, due to increased motor activity, can also have a positive effect on muscle tissue formation in pigs and, therefore, on the meat quality.

The absence of significant ($p < 0.05$) differences in a number of biochemical, morpho-hematological and other indicators of boars can be explained by the fact that their productivity realized in our experiment, i.e. the average daily live weight gain, was close to that genetically conditioned for the genotype F_2 (Large White × Landrace) × Duroc due to a balanced ration and an optimal microclimate. Under these conditions, only simulated social stress remained a factor influencing animals.

The absence of a significant difference, together with blood cortisol, TBARS and WA levels close to the control, in general, indicate the adaptation of boars to the cyclic long-term MS. However, the same groups differed in the blood glucose levels, LDH and CPK activity and dynamics, which indicates a better stress resistance of stressed animals when fed adaptogens. Note that when PSe was used as an adaptogen, these stress indicators turned out to be the highest, and in the group receiving DHQ, they were the lowest compared to both control groups. Similar results were obtained on broilers by Pirgoziev et al. [38] who found that dietary DHQ at different doses and/or under unfavorable conditions (for example, under heat stress) had positive effects, including an increase in the general antioxidant status [39].

Leveling stresses, in particular, stress of transportation, due to the dietary selenium additives was studied in pigs by Liu et al. [40]. Dietary selenium (0.24-1 mg/kg) and vitamin E (17-100 mg/kg) decreased hyperthermia in growing pigs [40]. Other studies dealt with the effect of dietary selenium on antioxidant status and meat quality [41-43]. In our study, we observed a positive effect of PSe on innate immunity, i.e. an increase in the blood bactericidal activity, and on hematological parameters, including an increase in the level of erythrocytes ($p < 0.05$), hemoglobin ($p < 0.05$) and hematocrit ($p < 0.01$) compared to the animals stressed but not fed adaptogens.

Our study is mainly focused on the effect of DHQ on biochemical, antioxidant and hormonal status of boars under MS. It should be mentioned that this issue has been little studied. Therefore, special attention should be paid to the works that reveal the physiological mechanisms of quercetin activity. Thus, it has been shown that the bioavailability of quercetin is due to the chemical form of flavonoids and dietary factors [44, 45]. Conjugated quercetin is the main metabolite in blood 24 hours after the intake of this supplement. The highest concentrations of quercetin and its metabolites were found in the liver and kidneys (5.87 and 2.51 nmol/g tissue, respectively), the organs responsible for the excretion of metabolic products, while the lowest in the brain, heart and spleen [46]. The blood level of quercetin in pigs after 3 days of consumption of high doses (up to 500 mg/kg) did not exceed 1.25 mmol/l [46, 47]. Also, no differences were found between long-term and repeated use compared to single application [48]. Of the dietary factors, the bioavailability of quercetin was influenced by the dietary fat content [45]. It was found that the combination of vitamin E with quercetin leads to the best positive effect [49]. Quercetin did not affect the activity of glutathione peroxidase, glutathione reductase, and glutamate-cysteine ligase in the mucous membrane of small intestine and liver of piglets after weaning, while the activity of hepatic glutathione transferase significantly increased on day 5 after weaning when quercetin was fed at 100, 300 и 900 mg/kg live weight [50]. Quercetin enhanced the protection of pig intestinal erythrocytes from oxidative stress [51]. It was found that when contaminated feed with mycotoxins, quercetin, alone or in

combination with vitamins and selenium, contributed to the partial restoration of the oxidative status [52], which is consistent with the data obtained and described above. In pigs, quercetin reduced the effect of transportation stress through a decrease in the amount of serum endotoxin, ROS, and malondialdehyde in the intestine, an increase in the size of the villi of the jejunum with a simultaneous decrease in the expression of inflammatory cytokines [53]. An increase in the adaptive capabilities of technologically stressed animals due to an antioxidant was noted, which is also consistent with the results of our studies.

Thus, dietary adaptogens, the Se proteinate (PSe) and especially dihydroquercetin (DHQ) prevent negative effect of modeling technological stress (MS) on metabolism in boars, including lipid peroxidation, stimulate anabolic processes, and positively affect clinical health and nonspecific resistance. The smallest concentration of cortisol, a hormone involved in the development of stress response, 134 nmol/l during intensive growth and 215 nmol/l during final fattening, was in pigs fed DHQ, the highest in pigs fed PSe during intensive growth (282 vs. 211 and 214 nmol/l in the control groups). The TBARS level which characterizes lipid peroxidation was the smallest (2.93 nmol/l) in boars fed DHQ during intensive growth and the highest (3.47 nmol/l) in the same group during final fattening. In boars fed DHQ, there was an increase in humoral immunity, that is, an increase in the levels of lysozyme (by 51.9%, $p < 0.05$) and lysis (by 19.22%, $p < 0.05$) compared to the control group 1 without MS. As a result, in different periods, the average daily weight gain of boars was 921-1103 g (+ PSe) and 950-1152 g (+ DHQ). In general, over the trials, the average gain was the greatest in the control (without stress) and in the stressed boars fed DHQ. Taken together, our findings indicate the promise of using PSe and DHQ in intensive pig rearing to level negative consequences of technological stresses and give grounds for further studying effects of these feed adaptogens for their proper use in intensive industrial pig breeding.

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