

THE EFFECT OF TWO DIFFERENT DOSES OF SELENIUM YEAST AND SODIUM SELENITE ON SELENIUM LEVEL IN BLOOD, COLOSTRUM, MILK AND METABOLIC PROFILE IN DAIRY COWS

¹**J. Illek**, Associate Professor MVDr., DrSc., Dipl. ECBHM,
Head of Department of Large Animal Clinical Laboratory
President of Czech Association for Buiatrics
<https://orcid.org/0000-0002-1374-7918>

¹University of Veterinary Sciences Brno, Czech Republic
E-mail: illekj@vfu.cz

²**D. Kumprechtová**, Ph. Dr., Researcher
<https://orcid.org/0000-0002-2591-9377>

²Institute of Animals Science Prague, Czech Republic
E-mail: dana.kumprechtova@gmail.com

³**V. A. Tomchuk**, Doctor of Veterinary Sciences, Professor,
Department of Animal Biochemistry and Physiology named after Academician M. F. Gulyi
<https://orcid.org/0000-0003-0622-6345>

³National University of Life and Environmental Sciences of Ukraine, Kyiv, Ukraine
E-mail: tomchuk_viktor@ukr.net

³**V. A. Gryshchenko**, Doctor of Veterinary Sciences, Professor,
Department of Animal Biochemistry and Physiology named after Academician M. F. Gulyi
<https://orcid.org/0000-0001-6601-1392>

³National University of Life and Environmental Sciences of Ukraine, Kyiv, Ukraine
E-mail: viktoriya_004@ukr.net

³**I. V. Kalinin**, Doctor of Biological Sciences, Professor,
Department of Animal Biochemistry and Physiology named after Academician M. F. Gulyi
<https://orcid.org/0000-0002-3740-7600>

³National University of Life and Environmental Sciences of Ukraine, Kyiv, Ukraine
E-mail: kalininihor@gmail.com

Abstract. The aim of the study was to compare effects of two levels of selenium yeast (SY) and sodium selenite (SS) supplementation on blood, colostrum and milk Se levels, blood chemistry parameters in dairy cows under field conditions.

The study included 36 Holstein cows from 5 weeks prepartum to 12 weeks postpartum. The cows were divided into 4 treatments (n = 9): 1. Negative Control (NC) – no Se supplement; 2. Positive Control (PC) – 0.3 ppm Se (from sodium selenite); 3. S1 – 0.3 ppm Se (from selenium yeast – SELSAF[®], Lesaffre Feed Additives, France); 4. S2 – 5 ppm Se (SELSAF[®], Lesaffre Feed Additives, France).

At 5 and 1 weeks prepartum, on the calving day, and 4, 8, 12 weeks postpartum, blood samples were taken. Colostrum and milk were collected on the calving day and 4, 8 and 12 weeks postpartum and analysed for Se content. Initial Se status in all the cows was marginal. Negative Control cows showed suboptimal blood Se levels for the whole period under study. S1 and S2 showed significantly (P < 0.01) higher values than NC and PC cows. Colostrum Se levels were significantly higher in S1 (128.17 ug/L) and S2 (155.58 ug/L) than in NC (94.68 ug/L) and PC (99.3 ug/L) cows.

Overall mean milk Se levels in S1 (20.4 ug/L) and S2 (50.0 ug/L) were higher than in NC (10.9 ug/L) and PC (16.6 ug/L). Biochemical indicators of blood did not significantly differ between the treatments and were within the physiological ranges.

Se levels in whole blood, colostrum and milk, and GSH-Px activity were significantly increased by selenium yeast supplementation. The response was dose dependent and consistent. Selenium from organic source was more bioavailable than selenium from sodium selenite. Dietary Se at a tolerance dose (5 ppm) had no detrimental effect on the blood chemistry parameters analysed.

Keywords: dairy cows, selenium, yeast, milk

Introduction

It is known that feeding organic Se to ruminants can increase the levels of Se in both colostrum and milk. This can have a two-fold benefit. Firstly, higher levels of Se are passed to suckling offspring,

increasing their Se status and optimising health, immunity and growth rates. Secondly, the resulting milk can be marketed as a value added food for the human market, as selenium is also an essential nutrient for human health (Surai, 2008).

Selenium is recognized as an essential trace element and its deficiency has been associated with impaired growth, fertility, and health in farm livestock (Schwarz and Foltz, 1957; Weiss et al., 1990). Selenium is extremely important for the proper postnatal development of the calf. In the first weeks of life, milk is the only source of Se for the calf. However, Se content in milk is rather low (Ortman and Pehrson, 1999), therefore calves from mothers with insufficient Se supplementation often suffer from myodystrophic diseases and other disorders later in their lives. The level of absorption and retention of microelements is modulated by their actual levels in the body and their concentrations in the diet and is generally higher for intake of their organic forms, i.e. those bound to aminoacids (Knowles et al., 1999). The absorption takes place in the small intestine. SeMet is efficiently absorbed via the methionine transporting system, whereas the absorption of sodium selenite is less efficient and occurs mainly by passive diffusion (Weiss, 2003).

Several studies have shown that Se from sodium selenite is poorly transferred to milk (Ortman and Pehrson, 1999) and that it is unable to maintain the Se status of nursing calves (Koller et al., 1984; Ortman and Pehrson, 1999). Dietary supplementation of selenium yeast to cows results in higher concentrations of Se in milk than inorganic Se supplementation (Aspila, 1991; Malbe et al., 1995; Ortman and Person, 1997; Ortman and Pehrson, 1999; Mahan, 2000; Givens et al., 2004).

Selenium is a natural antioxidant. As an integral part of the enzyme glutathione peroxidase (GSH-Px). Se functions to prevent oxidative damage to body tissues (Hoekstra, 1974; Gryshchenko et al., 2016). Many researchers demonstrated a positive correlation between Se concentrations and GSH-Px activity in blood.

The aim of this study was to investigate the effect of Se source on Se levels in blood, colostrum and milk of dairy cows and whether a high level of supplementation with organic Se does not induce blood and milk Se levels exceeding the physiological range; and what is the dynamic of changes of Se levels in colostrum and milk. Furthermore, the effects of supplementation with different forms and levels of Se on some blood chemistry parameters were investigated.

Materials and methods of research

Management, animals and feeding

The study was performed on a dairy farm with 640 Holstein crossbred cows basic herd with average milk yield of 10.500 kg. The cows were housed loose in pens by 30–40 heads, with straw bedding. Each pen was milked and fed separately, migration of animals between pens was excluded. Cows in the initial lactation phase (ca. 3 weeks post partum) were milked three times a day, others twice a day. The cows were fed total mixed ration TMR. For the diet composition and analytical values see Tables 1 and 2.

1. Diet composition

Feed (kg/day)	Dry cow diet	Close-up diet	Fresh cow diet	Lactation diet
Clover-grass silage	10	8	9	11
Peas silage	4	5	7	7
Maize silage	6	10	14	14
Maize silage (ears + leaves)	0	2	6	4
Sugar beet pulp	4	6	8	6
Yeast	0	3	3	3
Hey	3.5	1.5	1.5	2
Straw	3	1	0.3	1.0
Concentrate	1	3.5	7.5	4.5
Peas seed	0	0.3	0.5	0.5
Bearley meal	0	2	3	2
Mineral Feed Mikrop M5	0	0.16	0.16	0.16
Monophos	0.25	0	0	0
Sugar	0.3	0	0	0

2. Analysed diet nutrient contents

Nutrient	Unit	Dry cow diet	Close-up diet	Fresh cow diet	Lactation diet
----------	------	--------------	---------------	----------------	----------------

		in fresh matter	in dry matter	in fresh matter	in dry matter	in fresh matter	in dry matter	in fresh matter	in dry matter
Dry matter	%	46.01	100	47.58	100	47.97	100	49.74	100
Crude protein	%	5.67	12.33	7.18	15.09	7.82	16.31	8.74	17.56
Fat	%	1.03	2.24	1.70	3.57	1.91	3.98	2.12	4.26
Crude Fibre	%	11.07	24.06	9.75	20.49	8.56	17.84	7.63	15.33
Ash	%	2.86	6.22	3.64	7.65	3.86	8.05	4.09	8.22
Nitrogen-free extract	%	25.37	55.15	25.32	53.21	25.82	53.82	27.17	54.62
ME cattle	%	4.27	9.27	4.95	10.41	5.63	11.73	5.95	11.96
Calcium	g/kg	3.10	6.73	3.44	7.24	4.40	9.17	4.85	9.75
Phosphorus	g/kg	1.55	3.36	1.7	3.57	2.15	4.49	2.45	4.92
Sodium	g/kg	0.23	0.51	0.58	1.22	1.96	4.08	2.22	4.47
Magnesium	g/kg	0.94	2.04	1.14	2.40	1.44	3.01	1.70	3.41
Selenium	mg/kg	0.045	0,098	0.077	0,162	0.096	0,201	0.108	0,218

Experimental design

In the trial, 36 cows were included. There were four experimental treatments, 9 cows each.

From 5 weeks before the expected calving date to 12 weeks after the calving, the cows received the respective experimental diets: 1) Negative Control diet with no Se supplement; 2) Positive Control diet with sodium selenite – 0.3 ppm Se; 3) S2 diet with selenium yeast – 0.3 ppm Se; 4) S2 diet with selenium yeast – 5 ppm Se.

Se supplements were administered as top dressing on TMR in the trough. For PC, S1 and S2, the Se supplements were provided via a wheat flour-wheat bran premix. NC received a wheat flour – wheat bran premix with no Se source added.

A regular diet on the farm is supplemented with 0.3 ppm Se from an inorganic source (sodium selenite). The regular Se supplement was withdrawn from the diet one month before the start of the trial to induce a marginal selenium status in the cows.

The detailed time schedule of the trial was as follows:

All Treatments
Day 0: Beginning of experimental diets, selection of cows for the experimental treatments according to calving date, parity, previous lactation performance; Blood collection from all the cows for biochemistry (Se, GSH-Px, urea, CK, TP, albumin, GMT, AST, ALT, Vitamin E)
1 wk prepartum: Blood collection – Se, biochemistry
Calving: Blood collection – Se, biochemistry Colostrum collection – Se concentration
4 wk postpartum: Blood collection – Se, biochemistry Milk collection – Se concentration
8 wk postpartum Blood collection – Se, biochemistry Milk collection – Se concentration
12 wk postpartum Blood collection – Se, biochemistry Milk collection – Se concentration

Samplings and laboratory analyses

Blood samples were taken from the tail vein of all the cows, using the HEMOS kit (1 lithium heparine, 1 K₃EDTA, and 1 serum tube). Milk and colostrum were collected in sterile tubes. The samples were frozen

at – 18 °C and processed in the end of the study. The blood chemistry parameters measured included total protein (TP), albumine (Alb), creatin phosphokinase (CK), aspartate aminotransferase (AST), gamma-glutamyltrasferase (GMT), alanine aminotransferase (ALT), vitamin E, and glutathione peroxidase (GSH-Px). Standard analytical techniques were used for these analyses (Central Clinical Laboratories, University of Veterinary and Pharmaceutical Sciences, CZ). The concentrations of Se in whole blood, milk and feed were analysed with hydride generation atomic absorption spectrophotometry (HG-AAS) as described by Sturman (1958). At the start of the trial, feed analyses were performed.

The raw data were statistically processed with the software SPSS. The cow represented the unit for statistical analysis. Data except colostrum Se content, milk composition and production were analysed by a mixed repeated procedure. Colostrum Se content, milk composition and production data were analysed by a variance analysis (ANOVA). Results were declared as significant from $P < 0.1$.

Results of the research and their discussion

Blood chemistry parameters

The values of TP, urea, billirubin, AST, GMT, CK were within physiological ranges (Table 3). AST and GMT liver enzyme values were not apparently influenced by Se supplementation. CK activity decreased with increasing levels of organic Se, suggesting an improved muscle metabolism due to organic Se supplementation. These results are in accordance with those received by Juniper et al. (2006) who did not find any significant effect between with different levels of supplemental Se from Se yeast and the unslupplemented control, with the exception of blood urea and glucose values.

The values we found were generally within the expected normal range (Beers and Berkow, 1998).

3. Mean blood chemistry values from cows supplemented with selenite or two different levels of selenium yeast

Index	NC	PC	S1	S2	SE	P
Total protein, g/L	73.8	75.0	75.4	74.8	0.6	NS
Urea (mmol/L)	4.8	4.75	4.9	4.9	0.2	NS
Billirubin (µmol/L)	4.4	4.5	4.5	4.3	0.1	NS
Aspartate aminotransferase, ukat/L	1.5	1.5	1.5	1.5	0.0	NS
Gamma-glutamyltrasferase, ukat/L	0.4	0.4	0.4	0.4	0.0	NS
Creatin phosphokinase, ukat/L	3.3 ^b	4.7 ^a	2.8 ^{b^c}	2.0 ^c	0.4	<0.01

Notes: ^{a,b,c} Means within a line with different superscripts differ significantly.

gGSH-Px activity

The activity of the selenoenzyme glutathione peroxidase is often considered to reflect the selenium concentration in whole blood. This was the case in this study, too. Levels of GSH-Px in the SY supplemented groups were significantly higher already in the fourth week of the study (1 wk prepartum) ($P < 0.01$) and the SS supplemented group the GSH-Px values were significantly lower than those in the NC only 9 weeks from the start of supplementation (Table 4).

This increase seems to be earlier than that reported by Ortman and Perhson (1999) who noted that in a 12-wk study comparing the effect of Se source, the GSH-Px activity in cows receiving either selenate, SS or SY remained relatively constant for the first 6 wk of the study, but then increased markedly in wk 6 to 12, with the highest values noted for cows receiving the diet containing SY.

On the contrary, Juniper et al. (2006) did not receive any significant treatment effect for either source or concentration of dietary selenium on GSH-Px, but in their study 5 wk periods were used in the Latin square design which might have not be long enough for differences to develop. Similarly, out of 11 studies reviewed by Weiss (2003), 9 reported no significant difference in GSH-Px activity when comparing SY with SS.

4. Glutathione peroxidase activity in erythrocytes (ukat/L) of cows when supplemented with selenite or two different levels of selenium yeast

Treatment	NC	PC (0.3ppm Se)	S1 (0.3ppm Se)	S2 (5 ppm Se)	P
-----------	----	-------------------	-------------------	------------------	---

	GSH-Px (ukat/L)		GSH-Px (ukat/L)		GSH-Px (ukat/L)		GSH-Px (ukat/L)		
	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	
5 wk a.p.	701.69	22.13	606,52	59,57	658.31	58.43	640.04	47.48	
1 wk a.p.	688.48a	41.05	770,27ab	117,0	808.35b	81.88	1000.45c	89.05	< 0.01
Calving	692,20a	89.27	782,29a	96,48	968.51b	65.92	1062.96c	96.07	< 0.01
4 wk p.p.	687.40a	91.12	819,42b	70,84	1051.91c	111.09	1160.97d	71.87	< 0.01
8 wk p.p.	719,84a	4.28	826,15b	49,19	898.44c	322.79	1141.14d	94.61	< 0.01
12 wk p.p.	737,95a	108.62			1014.59b	44.84	1168.39c	94.58	< 0.01

Notes: ^{a,b,c,d} Means within a line with different superscripts differ significantly.

Selenium concentrations in blood

As shown in the Table 5, Se concentrations in blood in all the cows at the beginning of the trial, pre-supplementation, were suboptimal in all the experimental groups (NC – 69.06 ug/L, PC – 70.3 ug/L, S1 – 77.74 ug/L, S2 – 70.6 ug/L).

5. Mean whole blood selenium concentration for cows when supplemented with selenite or two different levels of selenium yeast

Treatment	NC		PC (0.3ppm Se)		S1 (0.3ppm Se)		S2 (5 ppm Se)		<i>P</i>
	Se (ug/L)		Se (ug/L)		Se (ug/L)		Se (ug/L)		
	mean	S.D.	mean	S.D.	mean	S.D.	mean	S.D.	
5 wk a.p.	69.16	5.0	70.3	5.7	77.7	7,3	70.6	6,7	
1 wk a.p.	68,2 ^a	6.2	90.8 ^a	7.0	97,7 ^b	7.7	155,0 ^c	22.1	< 0.01
Calving	67.0 ^a	5.6	93.6 ^b	7.9	109,1 ^c	7,9	152,2 ^d	16.5	< 0.01
4 wk p.p.	65.7 ^a	5.7	86.1 ^b	33.7	129,1 ^c	7.7	170,8 ^d	19.8	< 0.01
8 wk p.p.	68.9 ^a	4.3	105.1 ^b	7.0	128.6 ^c	11.2	184.4 ^d	9.9	< 0.01
12 wk p.p.	73,52 ^a	5.03	110.0 ^b	15.9	129,22 ^c	9.58	193,49 ^d	15.32	< 0.01

Notes: ^{a,b,c,d} Means within a line with different superscripts differ significantly.

The unsupplemented Negative Control cows showed suboptimal Se concentrations in blood for the whole experimental period, with the highest values in the weeks 8 and 12 postpartum (68.94 ug/L and 73.52 ug/L, respectively), but not significantly different.

The S1 (0.3 ppm Se as selenium yeast) and PC cows (0.3 ppm Se as sodium selenite) showed a steady increase in blood Se concentrations which were significantly higher ($P < 0.05$) than those of the NC. Mean values for the whole experimental period were 118 and 99 ug/L, respectively. Selenium concentration in blood of S1 cows was significantly higher than the one in PC cows ($P < 0.05$).

Se concentrations in blood of the S2 (5 ppm Se as Se yeast) cows was increasing quickly and already one week prepartum were more than twice as high as in the NC (68.18 vs. 155.09, $P < 0.01$). The blood Se concentrations were gradually increasing in S2 and reached 184.42 ug/L and 193.49 ug/L in the weeks 8 and 12 post partum, respectively. These values are relatively high and are considered as optimal by many scientists.

Similar benefits of SY over SS were reported by Fisher et al. (1995), Knowles et al. (1999), Pehrson et al., 1999, Juniper et al. (2006) and in the studies reviewed by Weiss (2003) who reported an overall mean 18% difference in blood Se concentrations between cows supplemented with equal amounts of Se yeast and sodium selenite in the studies reviewed.

The values received in this study were generally lower (even for the 5 ppm dose of Se from Se yeast) than those received by Juniper et al. (2006).

Selenium concentrations in colostrum and milk

As shown in Table 6, the differences in Se concentrations in colostrum between the experimental groups were considerable. As compared with the NC group (94.68 ug/L), Se colostrum concentrations were significantly ($P < 0.01$) higher with both the levels of SY (S1 – 128.17 ug/L; S2 – 155.58 ug/L), but not with SS as Se source.

6. Selenium concentrations in colostrum and milk for cows when supplemented with selenite or two different levels of selenium yeast

Treatment	NC		PC (0.3 ppm Se)		S1 (0.3 ppm Se)		S2 (5 ppm Se)		<i>P</i>
	Se (ug/L)		Se (ug/L)		Se (ug/L)		Se (ug/L)		
	mean	S.D.	mean	S.D.	mean	S.D.	mean	S.D.	
Calving	94.68 ^a	9.14	99,31 ^a	8,0	128.17 ^b	18.90	155,58 ^c	14.75	< 0.01
4 wk p.p.	10.10 ^a	3.38	15,93 ^b	2,22	21.24 ^b	2.46	37.01 ^c	14.84	< 0.01
8 wk p.p.	9.50 ^a	5.65	16,58 ^b	2,78	19.64 ^b	1.41	45.23 ^c	9.93	< 0.01
12 wk p.p.	9.09 ^a	5.21			20.06 ^b	2.16	56.49 ^c	24.53	< 0.01

Notes: ^{a,b,c}. Means within a line with different superscripts differ significantly.

Se concentrations in milk of the NC cows were low throughout the experimental period, there was not a great variation between the individual cows. The S1 cows showed significantly ($P < 0.01$) higher concentrations than the control ones. The S2 cows showed the highest values, significantly ($P < 0.01$) higher than the NC and S1. Cows receiving SS had significantly higher Se levels in milk, similar to those supplemented with the lower dose of SY.

An increase of Se in milk of animals supplemented with SY as compared with those supplemented with SS has been reported to range from 34% (Juniper et al., 2006) to 90% (Weiss, 2003).

It has been demonstrated that Se content in colostrum is higher than that in milk (Micetic-Turk et al., 2000; Pavlata et al., 2004).

Significantly higher concentration of Se in milk of dayir cows supplemented with selenium yeast were also reported by Givens et al. (2004), Juniper et al. (2006) and other researchers. As suggested by Pehrson (1993), the increased selenium concentration in milk derived from diets containign Se may be due to the preferential mammary gland uptake of SeMet, which is readily incorporated into milk protein (Juniper et al., 2006).

Conclusion

The study investigated the effect of dietary supplementation with two different levels of Se from selenium yeast (recommended and tolerance levels) and sodium selenite in selenium deficient dairy cows in the period from 5 weeks prepartum to 12 weeks postpartum on selenium levels in blood and milk and blood chemistry.

The results have shown that the Se levels in whole blood, colostrum and milk were significantly increased by SY supplementation. The GSH-Px activity was also significantly improved by SY supplementation. The response was dose dependent and consistent. Both the experimental doses eliminated selenium deficiency.

In this trial, Se from organic source – selenium yeast – was more bioavailable than selenium from inorganic source-sodium selenite.

References

- Aspila, P. (1991). Metabolism of selenite, selenomethionine and feed incorporated selenium in lactating goats and dairy cows. *Journal of agricultural science in finland*, 63, 1-74. doi: [10.23986/afsci.72394](https://doi.org/10.23986/afsci.72394)
- Beers, M. H., & Berkow, R. (1998). *The merck veterinary manual*. <http://www.merck.com> Accessed May 15, 2005.
- Fisher, D. D., Saxton, S. W., Elliott, R. D. & Betty, J. M. (1995). Effects of selenium sources on selenium status of lactating cows. *Veterinaiy clinical nutrition*, 2, 68–74. doi: [10.3168/jds.S0022-0302\(06\)72394-3](https://doi.org/10.3168/jds.S0022-0302(06)72394-3)
- Givens, D. I., Allison, R., Cottrill, B. & Blake, J. S. (2004). Enhancing the selenium content of bovine milk through alteration of the form and concentration of selenium in the diet of the dairy cow. *Journal of the science of food and agriculture*, 84, 811–817. doi: [10.1002/jsfa.1737](https://doi.org/10.1002/jsfa.1737)
- Gryshchenko, V. A., Chernyshenko, T. M., Gornitska, O. V., & Platonova, T. M. (2016). Evaluation of the functional state of liver and the efficiency of therapy for enteropathy of calves. *Fiziolohichniy Zhurnal*, 62(6), 102-109. doi: [10.15407/fz62.06.102](https://doi.org/10.15407/fz62.06.102)

Hoekstra, W. G. (1974). Biochemical role of selenium. Pages 61–77 in Trace element metabolism in animals, Vol. II. W. G. Hoekstra, J. W. Suttie, H. E. Ganther, and W. Mertz, ed. Univ. Park Press, Baltimore, MD.

Juniper, D. T., Phipps, R. H., Jones, A. K. & Bertin, G. (2006). Selenium supplementation of lactating dairy cows: effect on selenium concentration in blood, milk, urine and feces. Journal of dairy science, 89, 3544-3551. doi: [10.3168/jds.S0022-0302\(06\)72394-3](https://doi.org/10.3168/jds.S0022-0302(06)72394-3)

Surai, P. F. (2008). Increasing selenium levels in mil. Pages 325-327 in Current advances in selenium research and applications, Vol. I P.F. Surai, J.A. Taylor-Pickard, ed. Wageningen Academic Publishers

Koller, L. D., Whitbeck, G. A., & South, P. J. (1984). Transplacental transfer and colostrum concentrations of selenium in beef cattle. American journal of veterinary research, 45, 2507-2510. PMID: 6524746

Knowles, S. O., Grace, N. D., Wurms, K. & Lee, J. (1999). Significance of amount and form of dietary selenium on blood, milk, and casein selenium concentrations in grazing cows. Journal of dairy science, 82, 429–437.

Mahan, D. C. (2000). Effect of organic and inorganic selenium sources and levels on sow colostrum and milk selenium content. Journal of animal science, 78, 100-105. doi: [10.3168/jds.S0022-0302\(99\)75249-5](https://doi.org/10.3168/jds.S0022-0302(99)75249-5)

Malbe, M., Klaassen, M., Fang, W., Myllis, V., Vikerpuur, M., Nyholm, K., Sankari, S., Suoranta, K. & Sandholm, M. (1995). Comparisons of selenite and selenium yeast feed supplements on Se-incorporation, mastitis and leucocyte function in Se-deficient dairy cows. Journal of veterinary medicine, A 42, 111-121. doi: [10.1111/j.1439-0442.1995.tb00362.x](https://doi.org/10.1111/j.1439-0442.1995.tb00362.x).

Micetic-Turk, D., Rossipal, E., Kracher, M. & Li, F. (2000). Maternal selenium status in Slovenia and its impact on the selenium concentration of umbilical cord serum and colostrum. European journal of clinical nutrition, 54(6):522-524. doi: [10.1038/sj.ejcn.1601050](https://doi.org/10.1038/sj.ejcn.1601050)

Ortman, K., & Pehrson, B. (1997). Selenite and selenium yeast as feed supplements for dairy cows. Journal of veterinary medicine, A 44, 373-380. doi: [10.1111/j.1439-0442.1997.tb01121.x](https://doi.org/10.1111/j.1439-0442.1997.tb01121.x)

Ortman, K., & Pehrson, B. (1999). Effect of selenate as a feed supplement to dairy cows in comparison to selenite and selenium yeast. Journal of animal science, 77(12), 365-3370. doi: [10.2527/1999.77123365x](https://doi.org/10.2527/1999.77123365x)

Pavlata, L., Pechova, A. & Dvorak, R. (2004). Microelements in colostrum and blood of cows and their calves during colostrum nutrition. Acta veterinaria Brno, 73, 421-429. doi: [10.2754/avb200473040421](https://doi.org/10.2754/avb200473040421)

Pehrson, B. (1993). Selenium in nutrition with special reference to biopotency of organic and inorganic selenium compounds. Pages 71-89 in Proc. 9th Alltech Symp., Biotechnol. Feed Ind. T. P. Lyons, ed. Nottingham University Press, Nottingham, UK.

Pehrson, B., Ortman, K., Madjid, N. & Trafikowska, U. (1999). The influence of dietary selenium as selenium yeast or sodium selenite on the concentration of selenium in the milk of suckler cows and on the selenium status of their calves. Journal of animal science, 77, 3371-3376. doi: [10.2527/1999.77123371x](https://doi.org/10.2527/1999.77123371x)

Schwarz, K., & Foltz, C. M. (1957). Selenium as an integral part of factor 3 against dietary necrotic liver degeneration. Journal of the American Chemical Society, 79, 3292-3293. PMID: 10408880

Suzuki, K. T., & Ogra, Y. (2002). Metabolic pathway for selenium in the body: Speciation by HPLC-ICP MS with enriched Se. Food additives and contaminants. 19(10), 974-983. doi: [10.1080/02652030210153578](https://doi.org/10.1080/02652030210153578)

Weiss, W. P. (2003). Selenium nutrition of dairy cows: Comparing responses to organic and inorganic selenium forms. Pages 333-343 in Proc. 19th Alltech Annual Symp. Nutr., Biotechnol. Feed Food Ind. P. T. Lyons and K. A. Jacques, ed. Nottingham University Press, Nottingham, UK.

Weiss, W. P. (2005). Selenium sources for dairy cattle. Pages 61-72 in Proc. Tri-State Dairy Nutr. Conf., Ft. Wayne, IN. The Ohio State Univ., Columbus.

Weiss, W. P., Todhunter, D. A., Hagan, J. S. & Smith, K. L. (1990). Effect of duration of supplementation of selenium and vitamin E in periparturient dairy cows. Journal of dairy science, 73, 3187-3194. doi: [10.3168/jds.S0022-0302\(90\)79009-1](https://doi.org/10.3168/jds.S0022-0302(90)79009-1)

Wright, P. L., & Bell, M. C. (1966). Comparative metabolism of selenium and tellurium in sheep and swine. The American journal of physiology, 211(1), 6-10. doi: [10.1152/ajplegacy.1966.211.1.6](https://doi.org/10.1152/ajplegacy.1966.211.1.6)

Іллек Й., Кумпретова Д., Томчук В.А., Грищенко В.А., Калінін І.В. Вплив двох різних доз селено-містких дріжджів та селеніту натрію на рівень селену в крові, молозиві і молоці та металопрофіль у молочних корів (2021). Ukrainian Journal of Veterinary Sciences. Метою дослідження було порівняти вплив двох доз добавок селено-містких дріжджів (SY) та натрію

селеніту (SS) на рівень Se в крові, молозиві та молоці, біохімічні показники крові в молочних корів у польових умовах.

Дослідження включало 36 корів голштинської породи від 5 тижнів до отелення і 12 тижнів після них. Корів було поділено на 4 групи ($n = 9$): 1. Від'ємний контроль (NC) – без добавки Se; 2. Позитивний контроль (PC) – 0,3 проміле Se (з селеніту натрію); 3. Дослідна група S1 – 0,3 проміле Se (з селено-містких дріжджів – SELSAF®, кормові добавки Lesaffre, Франція); 4. Дослідна група S2 – 5 ppm Se (SELSAF®, кормові добавки Lesaffre, Франція).

Зразки крові від корів відбирали на 5 та 1 тижні до народження, у день отелення та на 4, 8 і 12 тижнів після отелення відбирали зразки крові. Молозиво і молоко вилучали в день отелення і на 4, 8 та 12 тижнів після нього і аналізували їх на вміст Se. Початковий рівень Se в крові корів усіх чотирьох груп був низьким. Впродовж усього досліджуваного періоду в крові корів групи NC спостерігався вихід рівня Se за оптимальні межі. У групах S1 і S2 встановлено вірогідно ($P < 0,01$) вищі його значення, ніж у корів NC і PC груп. Рівень Se у молозиві у корів груп S1 (128,17 мкг/л) і S2 (155,58 мкг/л) був значно вищим, ніж у корів груп NC (94,68 мкг/л) і ПК (99,3 мкг/л).

Загальний середній рівень Se в молоці корів дослідних груп S1 (20,4 мкг/л) та S2 (50,0 мкг/л) був вищим, ніж у контрольних групах NC (10,9 мкг/л) і ПК (16,6 мкг/л). Біохімічні показники крові тварин з різних груп істотно не відрізнялися і знаходилися в межах фізіологічних діапазонів.

Рівень Se в цільній крові, молозиві та молоці корів, а також активність глутатіонпероксидази значно підвищувалися за рахунок добавок селено-містких дріжджів. Відповідь організму була дозозалежною та опосередкованою. Селен з органічних джерел був біодоступнішим, ніж із селеніту натрію. Добавка Se з допустимою дозою (5 проміле) не мала негативного впливу на досліджувані біохімічні показники крові.

Ключові слова: молочні корови, селен, дріжджі, молоко

MORPHOLOGICAL AND BIOCHEMICAL PARAMETERS OF PIG BLOOD WHEN USED FEEDING FEED ADDITIVES LG-MAX AND SEL-PLEX

S. A. TKACHUK¹, *Doctor of Veterinary Sciences, Professor,
Department of Veterinary Hygiene named after Professor A. K. Skorokhodko*
<https://orcid.org/0000-0002-6923-1793>

¹*National University of Life and Environmental Sciences of Ukraine, Kyiv, Ukraine*
E-mail: ohdin@ukr.net

I. V. YATSENKO², *Doctor of Veterinary Sciences, Professor,
Department of Veterinary Sanitary Examination and Veterinary Forensic Medicine*
²*Kharkiv State Zooveterinary Academy, Kharkiv Oblast, Ukraine*
<https://orcid.org/0000-0001-8903-2129>

E-mail: yacenko-1971@ukr.net

L. V. TKACHYK¹, *Degree Seeker,
Department of Veterinary Hygiene named after Professor A. K. Skorokhodko*
<https://orcid.org/0000-0002-9136-2925>

¹*National University of Life and Environmental Sciences of Ukraine, Kyiv, Ukraine*
E-mail: tklu78@gmail.com

Abstract. *The article presents scientific research to determine the morphological and biochemical parameters of blood in young pigs and pigs for fattening for the use in the diet of organic feed additives «Lg-Max» and «Sel-Plex».*

Feed additives «Lg-Max» together with «Sel-Plex», was introduced as part of a premix to animal feed of the experimental group, taking into account the need of animals in ω -3 unsaturated fatty acids (daily requirement of pigs in ω -3 is 672 mg. In 1 g of experimental feed additive contains 353 mg of ω -3), and the drug «Sel-Plex» - in the amount of 0.5 mg/kg.

According to the results of the study, it was found that the studied morphological parameters of pig blood were within physiological limits according to age.

Biochemical parameters in the serum of the experimental group of pigs in comparison with the control of the corresponding age are in the following dynamics: in pigs of 45 days of age probably increases - the concentration of globulins; α ₂-globulins and β -globulins, and probably decreases the content of aspartate transaminase (AST); in pigs 120 days of age is likely to increase - the content of total protein and magnesium; probably decreases - the content of cholesterol and activity alkaline phosphatase; in 155-day-old pigs, the concentration of calcium probably increases, and the concentration of cholesterol probably decreases.

Key words: *young pigs, fattening pigs, morphological and biochemical parameters of blood, natural feed additives*

Introduction

Omega-3 fatty acids are important to reduce the risk of cardiovascular disease, can have long-term effects on the immune system and bone health, reduce the risk of cancer and mental illness in humans. Unfortunately, the consumption of ω -3 fatty acids is insufficient for humans, especially for the population of most industrialized countries. At the same time, meat and meat products do not contain enough ω -3 fatty acids, and pork is no exception. Therefore, enriching pork with ω -3 fatty acids may be an effective way to increase ω -3 fatty acid intake and may improve the ratio of ω -6 to ω -3 fatty acids or the ω -3 index in health-conscious consumers (Huang et al., 2021).

Fatty acids are chemically short-, medium- and long-chain. Short- and medium-chain fatty acids are absorbed directly into the blood through the capillaries of the intestinal tract and pass through the portal vein, along with other nutrients. Fatty acids with longer chains are too large to get directly through the small openings of the intestinal capillaries. Instead, they are absorbed by the fatty villi of the intestinal wall and re-synthesized into triglycerides. Short- and medium-chain fatty acids, regardless of their cellular signaling functions, are important substrates of energy metabolism and anabolic processes in mammals. Unlike long-chain fatty acids, their cellular metabolism depends on fatty acid-binding proteins. These acids modulate the

tissue metabolism of carbohydrates and lipids, which is manifested mainly by an inhibitory effect on glycolysis and stimulation of lipogenesis or gluconeogenesis. Also, they act in mitochondria without or weak protonophoric and lytic measures, and do not significantly impair electron transfer in the respiratory chain, and simulate the production of mitochondrial energy by two mechanisms: they provide a reduction in equivalents to the respiratory chain and partially reduce the efficiency of synthesis (Schönfeld & Wojtczak, 2016).

At the same time, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are those ω -3 fatty acids that are mainly found in fatty fish and fish oil. Functionally, they are able to act on the chemotaxis of leukocytes, the expression of adhesion molecules, the production of eicosanoids such as prostaglandins and leukotrienes, ie to promote the production of anti-inflammatory cytokines. The mechanism of anti-inflammatory action of EPA and DHA is based on a change in the composition of phospholipids of the fatty acid cell membrane, a decrease in the expression of inflammatory genes and the activation of the anti-inflammatory factor activated by the γ peroxisome proliferator (Calder, 2017; Tortosa-Caparrós et al., 2017; Cholewski et al., 2018).

It is known that feed additives with ω -3 improve the productivity and health of pigs. However, recent studies have shown that animal productivity is affected by feeding and the ratio of ω -6 to ω -3 fatty acids. The predominance of ω -6 fatty acids in the diet contributes to the development of many diseases, including cardiovascular, cancer, as well as inflammatory and autoimmune diseases. The optimal ratio of ω -6: ω -3 can suppress immune stimulation, providing more energy and nutrients for high productivity (Nguyen et al., 2020).

Analysis of recent research and publications

Evaluation of morphological and biochemical parameters of pig blood using different types of natural feed additives in pig feeding is a necessary study to establish scientific evidence of their effects on the body (Kluczek, 2006; Bondarenko, 2017; Hrushanska & Kostenko, 2017; Kucheriavyi & Boichuk, 2017).

The mechanisms of natural resistance are especially important - cellular and nonspecific humoral protection is provided by the circulatory system. The state of humoral mechanisms of natural resistance can be assessed by such indicators as: number of erythrocytes, hemoglobin concentration, number of leukocytes, leukocyte blood formula, concentration of total protein and protein fractions of blood, including albumins and globulins, of which α -, β - and γ -globulins. The morphological and biochemical composition of blood greatly affects the intensity of metabolic and redox processes in pigs, and which can be said about the intensity of metabolism, which in turn affects the level of their productivity. Metabolism is influenced by genotype, sex, age, level of feeding of animals, etc. (Stryzhak et al., 2014). Разом із тим, нині доведена дія препаратів які містять селен на різні вікові групи свиней, на тлі розвитку транспортного стресу, що характеризувалася зміною співвідношення різних форм лейкоцитів у крові, характерною для розвитку стадії резистентності стрес-синдрому та збільшенням кількості еритроцитів і лейкоцитів, вмісту гемоглобіну, та показнику гематокриту. Також, спостерігали зростання вмісту Т-лімфоцитів на 45,4% і В-лімфоцитів на 12,5%. У тварин на відгодівлі, яким попередньо вводили препарат, спостерігаються біохімічні зміни, пов'язані з підвищенням інтенсивності росту кісткової і м'язової тканини (Iefimov, 2015).

Also, the use of sodium selenite and its combination with an amino acid supplement in experimental groups of piglets led to an increase in the number of erythrocytes, hemoglobin concentration, due to increased redox processes, and also leads to increased protein content in the serum of piglets. albumin, but also due to the increase in the accumulation of globulins. At the same time, it has been shown that replacing inorganic selenium with organic in the diet of pigs can improve the quality of meat (Zhang et al., 2020).

A number of scientific studies have shown that feeding diets of pigs containing sufficient ω -3 fatty acids helped to reduce the concentration of low-density lipoproteins and triglycerides in the blood (Meadus et al., 2012; Liu & Kim, 2018).

At the same time, one study showed that the growth rates of pigs fed a omega-6 to omega-3 ratio of 5: 1 were the best. However, the group fed 1:1 ω -6 to ω -3 ratios had the highest muscle mass and the lowest adipose tissue mass. Such ratios of Omega-6 to Omega-3 had a positive effect on lipid metabolism and reduced inflammation, which led to a large amount of energy and nutrients to ensure high productivity and homeostasis (Li et al., 2015). Разом з тим, іншими дослідниками доказано, що залежно від кількості поліненасичених чи насичених жирних кислот у годівлі свиней їх буде різний вміст у м'язовій та жировій тканинах і буде збільшуватися середньодобовий приріст свиней на відгодівлі (Uradhaya et al., 2016).

The purpose of the study – to determine the morphological and biochemical parameters of blood in fattening pigs for the use of natural feed additives «Lg-Max» together with «Sel-Plex».

Materials and methods of research

The efficiency of using the studied additive «Lg-Max» together with «Sel-Plex» during fattening of young animals and pigs for fattening was evaluated on the basis of production indicators of LLC "Payovyk-C" of Pereyaslav-Khmelnyskyi district.

The following periods of pig breeding are used in the experimental farm: suckling period - 28 days; growing period - 30–90 days; fattening 90–180 days.

For research after a 15-day equalization period, groups of analogues (5 heads in the control and experimental groups) by origin, age and live weight were formed (Table 1).

The experimental groups were formed from wild boars – young castrated male pigs.

1. Scheme of scientific and economic experience

Group	Livestock of animals, heads	Periods (age, days)		
		comparative period (30–45)	growing (30–90)	fattening (90–180)
Control	5	MD	MD	MD
Experimental – D	5	(main diet)	MD +2,0 g supplements «Lg-Max» and «Sel-Plex» (0,5 МГ/КГ)	MD +2,0 g supplements «Lg-Max» and «Sel-Plex » (0,5 МГ/КГ)

Blood was collected from the marginal ear vein in the morning before feeding the pigs before the start of the study for 45-120- and 155 days, which coincided with the rearing periods.

Throughout the study period, the animals were fed twice a day with dry granular feed with free access to water.

Feed additives «Lg-Max» together with «Sel-Plex», was introduced as part of a premix to animal feed of the experimental group, taking into account the need of animals in ω -3 unsaturated fatty acids (daily requirement of pigs in ω -3 is 672 mg. In 1 g of experimental feed additive contains 353 mg of ω -3), and the drug «Sel-Plex» - in the amount of 0.5 mg/kg.

Serum was obtained from whole blood by centrifugation. Serum biochemical parameters were evaluated on an automatic biochemical analyzer GBG ChemWell 2910 (USA) and using a test system – Global Scientific (USA).

The obtained figures were statistically processed using the software package "Microsoft Excel" with the calculation of the arithmetic mean and its error ($M \pm m$), the level of probability (P) according to the Student's table ($P < 0.05$; $P < 0.01$; $P < 0.001$).

Results of the research and their discussion

Organic feed additive «Lg-Max» - powder (according to the Registration Certificate for the drug «Lg-Max»), owner - Alltech (USA), registered in Ukraine for № AA-05713-04-15 from 25.02.2015. This preparation contains algae *Schizochytrium limacium* and rosemary extract *Rosmarinum officinalis*. «Lg-Max» is a feed additive that is a source of replenishment of polyunsaturated fatty acids of the ω -3 class, namely docosahexaenoic, which promotes the development of the nervous system and brain of animals, improves skin and fur, enhances immunity and anti-inflammatory functions. Therefore, it is used for dogs and cats (Tkachyk & Tkachuk, 2019).

«Sel-Plex» is a source of organic selenium. It is produced by strains of yeast grown on a selenium-enriched medium with low sulfur content, which is constantly monitored. In the process of life, yeast uses selenium to form cellular components. The drug «Sel-Plex» contains 1000 mg/kg of selenium. Most of which (98%) are selenomethionine and selenocysteine.

The results of the study of the number of erythrocytes, leukocytes and hemoglobin in the blood of pigs according to the scientific and economic experiment are presented in Table 1.

When «Lg-Max» feed additive was used in pig feeding - 2.0 g/day together with «Sel-Plex» feed additive, the number of erythrocytes and leukocytes in the blood of pigs of the experimental groups, compared with the control, was within physiological limits according to age.

At the same time, on day 120, the number of erythrocytes in the blood of pigs of experimental group D significantly increased by 14.5% ($P < 0.05$) compared with the control.

At the same time, on day 45, the number of leukocytes in the blood of pigs of this experimental group significantly increased by 5.0% ($P < 0.05$) compared with the control.

1. Morphological parameters of pig blood with the use of feed additive «Lg-Max» (2.0) g and «Sel-Plex», $M \pm m$, $n=5$

Indicator	Control 45 дiб	D 45 дiб	Control 120 дiб	D 120 дiб	Control 155 дiб	D 155 дiб
Erythrocytes, $\times 10^{12}/L$	5.10 ± 0.33	5.60 ± 0.51	6.0 ± 0.31	$6.87 \pm 0.03^*$	6.15 ± 0.02	6.27 ± 0.05
Leukocyte, $\times 10^9/L$	13.6 ± 0.19	$14.28 \pm 0.20^*$	16.76 ± 0.11	16.96 ± 0.08	16.66 ± 0.19	16.9 ± 0.12
Hemoglobin, g/L	$115.6 \pm 0,6$	115.0 ± 0.48	136.6 ± 1.89	140.2 ± 0.58	144.96 ± 2.34	146.0 ± 0.71

Note: * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$, compared with the control of the corresponding age.

Although the number of leukocytes increased, it was within physiological limits in terms of their number – this may indicate the potential for immunomodulatory activity (Fentona et al., 2013; Roselli et al., 2017) of these feed additives in pigs. The reasons for this are not clear, but may be related to the content in the feed additive «Lg-Max» up to 56% eicosapentaenoic acid.

Table 2 shows the biochemical analysis of pig blood for use in feeding the feed additive «Lg-Max» (2.0 g/day) together with «Sel-Plex».

2. Biochemical parameters of pig serum with the use of feed additive «Lg-Max» (2.0 g/day + «Sel-Plex»), $M \pm m$, $n = 5$

Indicator	Control 45 days	Group				
		D 45 days	Control 120 days	D 120 days	Control 155 days	D 155 days
Total protein, g/L	51.24 ± 0.80	52.48 ± 0.35	73.00 ± 0.16	$74.12 \pm 0.45^*$	76.80 ± 0.81	75.36 ± 2.57
Albumin, % in particular:	57.94 ± 1.08	58.78 ± 1.87	52.60 ± 0.40	53.48 ± 0.24	48.60 ± 0.51	50.24 ± 1.62
α_1 -globulins, %	3.68 ± 0.24	3.56 ± 0.82	3.40 ± 0.40	4.00 ± 0.32	3.80 ± 0.37	3.68 ± 0.25
α_2 -globulins, %	16.40 ± 0.24	$15.46 \pm 0.24^*$	17.40 ± 0.51	16.80 ± 0.73	19.40 ± 1.50	19.09 ± 0.93
β -globulins, %	11.16 ± 0.24	11.56 ± 0.18	16.60 ± 0.51	15.80 ± 0.37	19.20 ± 0.86	17.51 ± 0.28
γ -globulins, %	10.82 ± 0.58	10.64 ± 1.07	10.00 ± 0.51	9.92 ± 0.49	9.00 ± 0.58	9.48 ± 1.52
A/G ratio	1.38 ± 0.03	1.43 ± 0.03	1.11 ± 0.23	1.15 ± 0.01	1.06 ± 0.02	1.01 ± 0.04
Glucose, mmol/L	6.26 ± 0.05	5.82 ± 0.51	6.94 ± 0.09	6.98 ± 0.12	6.46 ± 0.14	6.23 ± 0.05
Alanine transaminase, IU	41.00 ± 0.71	42.17 ± 0.34	46.20 ± 0.37	47.60 ± 1.21	46.80 ± 1.39	45.16 ± 2.43
Aspartate transaminase, IU	76.60 ± 1.47	$65.36 \pm 3.28^*$	66.40 ± 0.51	64.58 ± 0.75	63.60 ± 1.81	64.27 ± 2.31
Urea, mmol/L	2.72 ± 0.06	2.74 ± 0.06	4.68 ± 0.24	4.18 ± 0.16	4.72 ± 0.12	5.08 ± 0.16
Creatinin, $\mu\text{mol}/L$	102.20 ± 3.75	101.23 ± 1.89	116.0 ± 4.51	112.86 ± 2.43	162.00 ± 5.13	158.34 ± 4.98
Cholesterol, mmol/L	2.54 ± 0.16	2.63 ± 0.06	2.94 ± 0.07	$2.66 \pm 0.09^*$	2.94 ± 0.13	$2.04 \pm 0.15^{**}$
Alkaline phosphatase, IU	167.40 ± 2.09	164.38 ± 2.43	165.80 ± 1.94	$152.00 \pm 1.73^{***}$	155.20 ± 3.92	150.26 ± 4.72
Bilirubin, mmol/L	3.80 ± 0.49	4.26 ± 0.72	5.60 ± 0.24	6.12 ± 0.28	6.00 ± 0.71	6.79 ± 0.50
Amylase, IU	2145.20 ± 194.80	$2352.41 \pm$	$845.40 \pm$	$860.80 \pm$	$797.80 \pm$	$852.13 \pm$

		82.24	30.24	11.56	36.23	52.36
Calcium, mmol/L	2.45 ± 0.02	2.48 ± 0.03	2.50 ± 0.04	2.72 ± 0.15	2.42 ± 0.01	2.72 ± 0.03***
Phosphorus, mmol/L	1.72 ± 0.07	1.52 ± 0.16	2.00 ± 0.07	2.34 ± 0.14	2.42 ± 0.12	2.18 ± 0.14
Potassium, mmol/L	4.08 ± 0.18	4.97 ± 0.59	4.96 ± 0.07	4.72 ± 0.10	5.18 ± 0.08	5.38 ± 0.14
Iron, µmol/L	25.70 ± 0.60	24.61 ± 0.48	24.48 ± 0.78	25.10 ± 1.29	28.08 ± 0.01	29.43 ± 0.12***
Sodium, mmol/L	142.20 ± 1.07	138.46 ± 1.23	145.20 ± 0.86	142.80 ± 1.34	147.80 ± 1.36	149.54 ± 1.26
Chlorides, mmol/L	99.00 ± 1.09	98.07 ± 1.59	104.80 ± 1.39	100.80 ± 1.46	103.00 ± 0.71	101.58 ± 1.43
Magnesium, mmol/L	1.22 ± 0.11	1.18 ± 0.16	1.54 ± 0.12	2.48 ± 0.07***	1.88 ± 0.09	2.96 ± 0.38*

Note: * P < 0.05; ** P < 0.01; *** P < 0.001, compared with the control of the corresponding age.

According to the obtained results (Table 2) it follows that all studied biochemical parameters in the serum of pigs of the experimental group were within physiological limits according to the age of pigs. However, on day 45 in the blood of pigs of the experimental group the content of α_2 -globulins was lower by 5.7% (P < 0.05), compared with the control.

With the use of ω -3 polyunsaturated fatty acids in the feeding of pregnant sows and piglets. Thus, the addition of 1% of the supplement to the diet increased the ratio of ω -3: ω -6 in colostrum and milk compared to the control (P = 0.05). In the blood plasma of piglets on the 3rd day after weaning had a higher (P < 0.05) coefficient of polyunsaturated fatty acids ω -3: ω -6 compared with the control. Corticosteroid-binding globulin concentrations did not differ between groups. The result of the free cortisol index was lower (P = 0.02) compared to the control. These results suggest that the provision of ω -3 supplements for sows, from late pregnancy and lactation, may increase the ratio of ω -3: ω -6 in their offspring, which may improve growth and reduce the acute physiological response to stress in pigs after weaning (McAfee et al., 2019).

The serum content of AST in the pigs of the experimental group was significantly lower by 1.52% (P < 0.05) compared with the control group. These enzymes are catalysts for the amine group transfer reaction between amino and keto acids, resulting in the formation of new amino acids, ie protein synthesis. The higher their concentration, the higher the activity of a particular metabolic process, the more active the enzyme, the more intense are the metabolic processes in the body (Bondarenko, 2017).

For the rest of the biochemical parameters in the blood serum of pigs of the experimental group compared with the control, there was a tendency to change.

In particular, the stability of blood glucose indicates insulin resistance. Thus, a study of the acute effect of eicosapentaenoic acid on glucose homeostasis focused on the role of free fatty acid receptor 1 (FFAR1) and the chronic effect of ω -3 fatty acids on fish oil on insulin resistance. Insulin resistance was induced by feeding mice a high-fructose, fatty diet (HFrHFD) for 16 weeks. In the first part, the acute effect of eicosapentaenoic acid alone and in combination with GW1100 and DC260126 (FFAR1 blockers) on hepatic homeostasis and hepatic phosphatidyl-inositol-4,5-bisphosphate. In the second part, the mice were treated with fish oil and ω -3 fatty acids for 4 weeks, starting at 13 weeks of HFrHFD feeding. At the end of the experiment, changes in markers of resistance to blood and liver tissue and insulin signals FFAR1 were recorded. The results showed that the presence of eicosapentaenoic acid affected blood glucose levels at 0 and 30 minutes after glucose loading in SCD-fed mice, but improved glucose tolerance in HFrHFD-fed mice. Moreover, FFAR1 blockers reduced the effect of eicosapentaenoic acid on glucose tolerance and hepatic PIP2 and DAG levels. On the other hand, chronic consumption of ω -3 fatty acid fish oil reduced serum insulin and triglyceride levels without improving the insulin resistance index. In addition, they increased the levels of β -arrestin-2, PIP2 and pS473 in the liver, but decreased the level of DAG. Thus, the presence of eicosapentaenoic acid in the diet dramatically improved glucose homeostasis in HFrHFD-fed mice by modulating FFAR1 activity (El-Fayoumi et al., 2020).

According to the results shown in Table 2, it was found that on day 120 of the study, the content of total protein in the serum of pigs of the experimental group was significantly higher by 1.53% (P < 0.05), compared with the control. At the same time, the indicators of cholesterol and alkaline phosphatase content in the serum of pigs of the experimental group were significantly lower by 9.52 (P < 0.05) and 8.32% (P < 0.001), compared with the control, respectively. Instead, one of the trace elements, the content of which in the serum of pigs of the experimental group for 120 days was 61.0% (P < 0.001) significantly higher than the control – is Magnesium.

Subsequently, for 155 days (Table 2) in the serum of pigs of the experimental group, the concentration of cholesterol was significantly lower by 30.0% ($P < 0.01$), and the level of Calcium was higher by 12.4% ($P < 0.001$), compared with the control. The reduction of cholesterol in the blood of pigs occurs during the use of fermented feed and the beginning of lipid deposition in the fat depot, and therefore in the serum of these animals they are found in smaller quantities (Derzhovskiy, 2008; Kovalenko et al., 2010).

Other researchers have found that ω -3 polyunsaturated fatty acids can improve lipid and glucose homeostasis and prevent inflammation in animals. Little is currently known about the effect of ω -3 polyunsaturated fatty acids on the expression of adipocytokines and the accumulation of biologically active lipids under the influence of obesity caused by a diet high in fat. The experiments were performed on Wistar rats, divided into three groups: standard diet-control (SD), high-fat diet (HFD) and high-fat diet + fish oil (HFD + FO). The concentration of glucose and insulin in fasting plasma was investigated. The addition of fish oil significantly reduced the plasma insulin concentration and the index of the homeostatic model of insulin resistance (HOMA-IR) and reduced the content of biologically active adipose tissue lipids. Supplements of ω -3 polyunsaturated fatty acids have improved insulin sensitivity, can prevent the development of insulin resistance in response to high-fat feeding, and can regulate the expression and secretion of adipocytokines in animals (Chacińska et al., 2019).

At the same time, the levels of iron and magnesium in the serum of pigs of the experimental group were significantly higher by 4.81 ($P < 0.001$) and 57.4% ($P < 0.05$), compared with the control, respectively.

From scientific sources it is known that Calcium and Magnesium are necessary in the body for the normal functioning of the nervous system, namely, to regulate the conduction processes of nerve endings and muscle contractions. These elements are involved in the formation of bone tissue, have a positive effect on cardiac activity and play an important role in blood coagulation. Phosphorus and Magnesium promote calcium metabolism. The main function of Phosphorus is that it transfers biological energy, partly from ATP. Magnesium is an extracellular ion and plays a major role for many enzymes, namely those involved in the transport of phosphates, which are of great energy importance (Yefimov et al., 2009). However, supplementation with minerals such as chromium and magnesium can help increase muscle tissue and reduce fat deposition in meat due to the effects of redistribution of nutrients that affect carbohydrate and lipid metabolism (Apple et al., 2000). Magnesium supplements before slaughter have also been shown to reduce the effects of stressors, reducing the release of catecholamines and cortisol, muscle relaxation and reduced neuromuscular stimulation, preventing a sharp drop in muscle pH after slaughter. Thus, the use of magnesium and selenium associated reduces the amount of lipids, helping to improve the lipid profile of pork for human consumption, without adversely affecting the quality and preservation, and it can be used as a tool to improve the nutritional aspects of pork (Carneiro de Albuquerque et al., 2019).

Conclusions and future perspectives

When used in the feeding of young pigs and pigs for fattening of the natural feed additives Lg-Max together with Sel-Plex studied morphological parameters of pig blood were within physiological limits according to age.

Biochemical parameters in the serum of the experimental group of young pigs and pigs for fattening compared with the control of the appropriate age are in the following dynamics:

– in the age of 45 days the concentration of α 2-globulins was lower by 5.7% ($P < 0,05$) and the content of AST - by 1,52% ($P < 0,05$);

– in 120 days of age probably increases - the content of total protein by 1.53% ($P < 0.05$), and magnesium - by 61.0% ($P < 0.001$); probably decreases – the content of cholesterol and alkaline phosphatase by 9.52 ($P < 0.05$) and 8.32% ($P < 0.001$);

– in 155 days, the concentration of calcium probably increases by 12.4% ($P < 0.001$) and the concentration of cholesterol probably decreases by 30.0% ($P < 0.01$);

In the future, it is planned to investigate the effect of these feed additives on the content of ω -3 fatty acids in the subcutaneous fat of pigs for fattening.

References

Apple, J. K., Maxwell, C. V., Rodas, B., Watson, H. B., & Johnson, Z. B. (2000). Effect of magnesium mica on performance and carcass quality of growing-finishing swine. *Journal of Animal Science*, 78(8), 2135–2143. doi: 10.2527/2000.7882135x

- Bondarenko, V. V. (2017). Vykorystannia bilkovo-vitaminnoi mineralnoi dobavky «MINAKTYVIT» v hodivli molodniaku svynei [Use of protein-vitamin mineral supplement "MINACIVIT" in feeding young pigs]: avtoref. dys. ... k-ta s/h. nauk: 06.02.02 / Bila Tserkva, 19. (in Ukrainian).
- Carneiro de Albuquerque, T. M. N., Ramos, E. M., Fiche da Matta Machado, I. F., Borges, P. C., Bolletta, A. G., Marcal, J. O., Carvalho, F. P., & Faria, P. B. (2019). Lipid profile and quality of meat from finishing pig supplemented with minerals. *Food Science of the Technology*, 39(3), 721-728. doi: 10.1590/fst.06118
- Calder, P. C. (2017). Omega-3 fatty acids and inflammatory processes: from molecules to man. *Biochem Soc Trans*, 45(5), 1105-1115. doi: 10.1042/BST20160474
- Cholewski, M., Tomczykowa, M., & Tomczyk, M. (2018). Comprehensive review of chemistry, sources and bioavailability of omega-3 fatty acids. *Nutrients*, 10(11), 1662. doi:10.3390/nu10111662.
- Chacińska, M., Zabielski, P., Książek, M., Szałaj, P., Jarzabek, K., Kojta, I., Chabowski, A., & Błachnio-Zabielska, A. U. (2019). The impact of omega-3 fatty acids supplementation on insulin resistance and content of adipocytokines and biologically active lipids in adipose tissue of high-fat diet fed rats. *Nutrients*, 11(4), 835. doi: 10.3390/nu11040835
- Derzhovskiy, O. O. (2008). Fizyko-khimichni vlastyivosti svynyny pry vykorystanni homohenizovanoho kormu [Physico-chemical properties of pork when using homogenized feed.]. *Problemy zootekhnologii ta veterynarnoi medytsyny. Zbirnik naukovih prac*, 16(41), 1, 206 – 210. (in Ukrainian)
- El-Fayoumi, S. H., Mahmoud, A. A. A., & Fahmy, A. (2020). Effect of omega-3 fatty acids on glucose homeostasis: role of free fatty acid receptor 1. *Naunyn-Schmiedeberg's Archives of Pharmacology*, 393, 1797-1808. doi: 0.1007/s00210-020-01883-5
- Fentona, J. I., Hord, N. G., Ghosh, S., & Gurzell E. A. (2013). Immunomodulation by dietary long chain omega-3 fatty acids and the potential for adverse health outcomes. *Prostaglandins, Leukotrienes and Essential Fatty Acids*, 89(6), 379–390. doi: 0.1016/j.plefa.2013.09.011
- Huang, C., Chiba, L. I., & Bergen, W. G. (2021). Bioavailability and metabolism of omega-3 polyunsaturated fatty acids in pigs and omega-3 polyunsaturated fatty acid-enriched pork: A review. *Livestock Science*, 243, 104370. doi: 10.1016/j.livsci.2020.104370
- Hrushanska, N. H., & Kostenko, V. M. (2017). Biokhimichni pokaznyky krovi svynomatok za profilaktyky porushen obminu mineralnykh rehovyn [Biochemical parameters of sow blood for prevention of violations of mineral metabolism]. *Naukovi visnyk LNUVMB imeni S.Z. Gzhytskoho*. 19. 82. 71–76.
- Iefimov, V. H. (2015). Biokhimichni pokaznyky krovi svynei na riznykh etapakh vyroshchuvannia za vplyvu vitaminu E i selenu [Biochemical parameters of blood of pigs at different stages of cultivation under the influence of vitamin E and selenium]. *Naukovo-tekhnichnyi biuleten DNDKI vetpreparativ ta kormovykh dobavok i Instytutu biolohii tvaryn*, 16(2), 23-29 (in Ukrainian).
- Kucheriavyyi, V. P., & Boichuk, V. M. (2017). Pokaznyky krovi vidhodivelnoho molodniaku svynei pry zghodovuvanni pro biotychnoho preparatu. [Indicators of blood of fattening young pigs when fed on a biotic preparation]. *Ahrarna nauka ta kharchovi tekhnolohii tekhnolohiia kormiv*, 4(98), 34-40. (in Ukrainian).
- Kovalenko, V. F., Zinov'ev, S. G., Bindyug, A. A. & Ban'kovskaya, I. B. (2010). Novye fermentirovannyye kormovyye dobavki v svinovodstve [New fermented feed additives for pig production]. *Zootekhnika*, 1, 18-19.
- Liu, W. C., & Kim, I. H. (2018). Effects of different dietary n-6:n-3 PUFA ratios on growth performance, blood lipid profiles, fatty acid composition of pork, carcass traits and meat quality in finishing pigs. *Annals of Animal Science*, 18(1), 143-154. doi: 10.1515/aoas-2017-0026
- Li, F., Duan, Y., Li, Y., Tang, Y., Geng, M., Oladele, O. A., Kim, S. W., & Yin, Y. (2015). Effects of dietary n-6:n-3 PUFA ratio on fatty acid composition, free amino acid profile and gene expression of transporters in finishing pigs. *British Journal of Nutrition*, 113(5), 739-748. doi: 10.1017/S0007114514004346
- McAfee, J. M., Kattesh, H. G., Lindemann, M. D., Voy, B. H., Kojima, C. J., Burdick Sanchez, N. C., Carroll, J. A., Gillespie, B. E., & Saxton, A. M. (2019). Effect of omega-3 polyunsaturated fatty acid (n-3 PUFA) supplementation to lactating sows on growth and indicators of stress in the postweaned pig. *Journal of Animal Science*, 97(11), 4453-4463. doi: 10.1093/jas/skz300
- Meadus, W. J., Duff, P., Rolland, D., Aalhus, J. L., Uttaro, B., & Russell, M. E. (2012). Dugan feeding docosahexaenoic acid to pigs reduces blood triglycerides and induces gene expression for fat oxidation. *Canadian Journal of Animal Science*, 91(4), 601-612. doi:10.4141/cjas2011-055
- Nguyen, D. H., Yun, H. M., & Kim, I. H. (2020). Evaluating impacts of different omega-6 to omega-3 fatty acid ratios in corn–soybean meal-based diet on growth performance, nutrient digestibility, blood

- profiles, fecal microbial, and gas emission in growing pigs. *Animals*, 10(1), 42. doi: 10.3390/ani10010042
- Roselli, M., Pieper, R., Rogel-Gaillard, C., Vries, H., Bailey, M., Smidt, H., & Lauridsen, C. (2017). Immunomodulating effects of probiotics for microbiota modulation, gut health and disease resistance in pigs. *Animal Feed Science and Technology*, 233, 104-119. doi: 10.1016/j.anifeedsci.2017.07.011.
- Schönfeld, P., & Wojtczak, L. (2016). Short and medium-chain fatty acids in energy metabolism: the cellular perspective. *Journal Lipid Research*, 57(6), 943–954.
- Stryzhak, T. A., Khalina, L. V., Zakharov, V. V., & Nahorni, S. A. (2014). Hematologichni pokaznyky yak osoblyvosti interiernoho statusu svynei u selektsiino-pleminni roboti [Hematologic indices as features of the interior status of pigs in breeding and breeding work] *Visnyk Kharkivskoho natsionalnoho tekhnichnoho universytetu silskoho hospodarstva imeni Petra Vasylenka*, 144, 212–217. Available at: http://nbuv.gov.ua/UJRN/Vkhdtusg_2014_144_40. (in Ukrainian)
- Tkachuk, L. V., & Tkachuk, S. A. (2019). Biokhimichni pokaznyky syrovatky krovi svynei za zastosuvannya u hodivli orhanichnoi kormovoi dobavky LG-MAX. [Biochemical parameters of pig serum for use in feeding of organic feed additive LG-MAX]. *Naukovi dopovidi NUBiP Ukrainy*, 1(77), doi: 10.31548/dopovidi2019.01.02. (in Ukrainian).
- Tortosa-Caparrós, E., Navas-Carrillo, D., Marín, F. & Orenes-Piñero, E. (2017). Anti-inflammatory effects of omega 3 and omega 6 polyunsaturated fatty acids in cardiovascular disease and metabolic syndrome. *Critical Reviews in Food Science and Nutrition*, 57(16), 3421-3429. doi: 0.1080/10408398.2015.1126549
- Upadhaya, S. D., Li, T. S., & Kim, I. H. (2016). Effects of protected omega-3 fatty acid derived from linseed oil and vitamin E on growth performance, apparent digestibility, blood characteristics and meat quality of finishing pigs. *Animal Production Science*, 57(6), 1085-1090. doi: 10.1071/AN15641
- Yefimov, V. H., Kostiushevykh, K. L., & Sidletska, I. R. (2009). Vplyv vitaminu E, selenu ta L-karnitynu na morfolohichni sklad krovi knurtsiv na tli transportnoho stressu [Influence of vitamin E, selenium and L-carnitine on the morphological composition of boar blood against the background of transport stress]. *Naukovyi visnyk Lvivskoho NUVMBT imeni S. Z. Hzhyskoho*, 11, 2(41), 2, 96-99. (in Ukrainian).
- Zhang, S., Xie, Y., Li, M., Yang, H., Li, S., Li, J., Xu, Q., Yang, W., & Jiang, S. (2020). Effects of different selenium sources on meat quality and shelf life of fattening pigs. *Animals*, 10(4), 615. doi: 10.3390/ani10040615

МОРФОЛОГІЧНІ ТА БІОХІМІЧНІ ПОКАЗНИКИ КРОВІ СВИНЕЙ ПРИ ЗАСТОСУВАННІ В ГОДІВЛІ КОРМОВИХ ДОБАВОК LG-MAX І СЕЛ-ПЛЕКС

С. А. Ткачук, І. В. Яценко, Л. В. Ткачук

Анотація. У статті представлені результати визначення морфологічних і біохімічних показників крові у молодняку свиней та свиней на відгодівлі при застосуванні до раціону органічних кормових добавок Lg-Max і Сел-Плекс.

Кормові добавки Lg-Max разом із Сел-Плекс вводили у складі преміксу до комбікорму для тварин дослідної групи, з урахуванням забезпечення потреби тварин в ω -3 ненасичених жирних кислотах (добова потреба свиней у ω -3 становить 672 мг. У 1 г дослідної кормової добавки міститься 353 мг ω -3), а препарат Сел-Плекс – у кількості 0,5 мг/кг.

За результатами дослідження встановили, що досліджувані морфологічні показники крові свиней були у фізіологічних межах відповідно віку.

Біохімічні показники у сироватці крові дослідної групи свиней порівняно з контрольною відповідного віку знаходяться у наступній динаміці: у свиней 45-добового віку вірогідно підвищується – концентрація глобулінів; α_2 -глобулінів і β -глобулінів, а вірогідно знижується активність аспаратамінотрансферази (АСТ); у свиней 120-добового віку вірогідно підвищується – вміст загального білка і магнію; вірогідно знижується – вміст холестеролу та активність лужної фосфатази; у свиней 155-добового віку вірогідно підвищується – концентрація кальцію, а вірогідно знижується – концентрація холестеролу.

Ключові слова: молодняк свиней, свині на відгодівлі, морфологічні та біохімічні показники крові, натуральні кормові добавки

MODERN CALF REARING SYSTEM

V. F. RADCHIKOV¹, Doctor of Agricultural Sciences, Professor, Chief of Laboratory for Feeding and Physiology of Cattle Nutrition

<https://orcid.org/0000-0003-4090-6635>

E-mail: arud22222@gmail.com

D. M. BOGDANOVICH¹, Ph.D. of Agricultural Sciences, Associate Professor, Director General

<https://orcid.org/0000-0002-7272-3510>

E-mail: dmb787887@gmail.com

A. N. KOT¹, PhD of Agricultural Sciences, Associate Professor, Research Associate of Laboratory for Feeding and Physiology of Cattle Nutrition

<https://orcid.org/0000-0003-0719-9166>

E-mail: kan88@tut.by

V. P. TSAI¹, PhD of Agricultural Sciences, Associate Professor, Research Associate of Laboratory for Feeding and Physiology of Cattle Nutrition

<https://orcid.org/0000-0002-1603-557X>

E-mail: vzai@tut.by

V. A. TOMCHUK², Doctor of Veterinary Sciences, Professor, Head of Department of Biochemistry and Physiology of Animals named after Academician M. F. Gulyi

<https://orcid.org/0000-0002-9009-5554>

E-mail: tomchuk_viktor@ukr.net

V. A. GRYSHCENKO², Doctor of Veterinary Sciences, Professor, Professor of Department of Biochemistry and Physiology of Animals named after Academician M. F. Gulyi

<https://orcid.org/0000-0001-6601-1392>

E-mail: viktoriya_004@ukr.net

V. I. KARPOVSKIY², Doctor of Veterinary Sciences, Professor, Professor of Department of Biochemistry and Physiology of Animals named after Academician M. F. Gulyi

<https://orcid.org/0000-0003-3858-0111>

E-mail: karpovskiy@nubip.edu.ua

V. O. TROKOZ², Doctor of Agricultural Sciences, Professor, Professor of Department of Biochemistry and Physiology of Animals named after Academician M. F. Gulyi

<https://orcid.org/0000-0001-8619-195X>

E-mail: trokoz@nubip.edu.ua

¹Republican Unitary Enterprise Research and Practical Center of the National Academy of Sciences of Belarus for Animal Breeding, Zhodino, Belarus

²National University of Life and Environmental Science of Ukraine, Kyiv, Ukraine

Abstract. Calf rearing is critical to a successful dairy or beef cattle breeding. Maximum productivity at the lowest cost can be obtained from healthy calves only.

Zootechnical, biochemical and economic research methods were used during the experiments.

It has been determined that feeding calves with experimental milk replacer with milk period duration of 65 days allowed to obtain 692 g of the average daily weight gain for the experiment period, that is 2.3% lower than the control indicator. Feeding calves with WMR helps to reduce the cost of diet by 6.0% and the price cost of weight gain by 3.6%.

Use of dry skimmed milk replacer and whole milk replacer during the rearing period, with milk period duration of 115 days, contributed to decrease in weight gain by 1.8 and 1.2% compared to the control variant. Feeding calves with DSMR and WMR helped to reduce the cost of diet by 10.3 and 5.8% and the price cost of weight gain by 8.5 and 4.8%.

Feeding with DSMR and WMR in diet for young animals over 115 days of age during the post-milk period increases concentration of erythrocytes in blood by 10.0 and 9.8%, hemoglobin - by 5.8 and 3.9%, amount of glucose - by 11.0 and 9.5%.

Inclusion of DSMR and WMR in diet for young cattle with milk period duration of 65 and 115 days contributed to increase in the average daily weight gain in the post-milk period by 9.2 and 10.7%, while reducing the cost of feed by 5.8 and 7.6%, price cost of weight gain by 6.1 and 7.7% and increase in additional profit in the amount of 8.35 (3.5 USD) and 10.58 (4.5 USD) rubles per animal during

experimental period.

In the future, it is necessary to improve the feeding system of young cattle using new developments in this area.

Keywords: *young cattle, whole milk, whole milk replacer, dry skimmed milk replacer, hematological indicators, productivity, efficiency.*

Introduction

System of young cattle rearing consists of three technological periods: growing, rearing, fattening, which include the milk and post-milk period, period of intensive growth and the final fattening. Rearing calves using modern technology, feed and feed additives is critical for a successful dairy or beef cattle breeding. Maximum productivity at the lowest cost can be obtained from healthy calves only. In this regard, it is necessary to constantly improve the calves feeding system and develop new feed additives (Marques et al., 2019).

Analysis of recent research and publications

Digestive system of newborn calves is characterized by incomplete development: they have poorly developed proventricles: in the first three weeks of a calf's life, the ratio of rumen and abomasum volumes is 1:2; 6 weeks of age – 2:3; 8 weeks – 3:2; 10 weeks – 2:1. In an adult animal, the abomasum makes only 8% of the total stomach capacity, while the rumen is 80% (Antonovich, 2019).

Liquid milk feed is used as the main feed during the milk period for calves feeding, the rest of the diet consists of concentrates, hay or grass cutting. Feeding young calves should ensure a rational combination of high-grade nutrition like a monogastric animal, while simultaneously stimulating the development of proventriculus function in a targeted manner (Radchikova et al., 2018; Boorboor et al., 2020).

After birth, the calf needs to be fed with colostrum as early as possible and should receive it within 7-10 days, and then collected milk or milk of the nursing cows. At the most farms, whole milk or milk replacers are fed to calves. When using whole milk and skimmed milk replacer, whole milk is fed during 1-2 months, and skimmed milk is fed up to 4-5 months of age. It is required to feed milk at the rate of 1 liter per 5-6 kg of body weight of animal up to 10 days of age 4 times a day, and 3 times after. The maximum daily milk feedings fall on 2-3 decades, after that it is constantly reduced (Buryakov et al., 2019; Liu Ting et al., 2020; Lopez et al., 2020;).

When rearing young calves using liquid feed in large quantities, which are most attractive to their taste, animals eat relatively less of dry feed which delays development of proventriculus (Jiang et al., 2020; Radchikova et al., 2020; Rai et al., 2020; Turini et al., 2020).

From birth to 6 months of age, calves grow vigorously, skeleton, muscular system and internal organs are formed for which requires a certain amount of energy, nutrients and biologically active substances.

Up to 2 months of age, calves should receive feed with a high biological value of proteins, until the rumen is underdeveloped and synthesis of microbial protein in the proventriculus is absent or very weak. During this period, it is almost impossible to provide calves with full-grade protein with no milk feeding. With development of the proventriculus, a variety of plant food also become sources of protein (Sintzerova et al., 2019).

In the post-milk period, young animals are transferred to vegetable feed. The main challenges of this period: formation of animals of the desired type; achieving high body weight and condition (Gading et al., 2020; Shiasi Sardoabi et al., 2021).

During this period, different feeding systems can be used: uniform feeding throughout the year, when animals are fed with balanced mono feed, consisting of crushed and mixed different types of feeds in predetermined proportions, or seasonal feeding with a set of appropriate feeds. Typically, feeding programs are designed to use 3-4 types of feed to obtain feed mixtures (Dolzenkova, 2016; Smynev et al., 2017; Dalla, 2020).

When rearing calves, there are four main periods:

- milk period, starting from birth of calf and up to 3-4 months of age;
- post-milk period – from 3-4 to 6 months of age;
- period of intensive growth – from 6 months to 1 year of age;
- the period of final fattening – from 1 to 1.5 years of age.

Rearing calves up to 6 months of age is carried out according to feeding schemes with a set of diets for each decade. This is due to the fact that calves grow quickly, they need frequent diet changes. In addition,

dairy and concentrated feeds are used for calves, consumption of those is planned in advance. Costs of rearing young stock when using pure milk feeding programs are quite high. One calf usually requires 250-500 kg of whole milk to feed. Consumption of significant amounts of milk for feeding young animals, along with rise in cost of rearing animals, leads to sharp decrease in marketability of milk and excludes it from the field of direct human use.

Inclusion of whole milk replacers (WMR) in diet for calves allows to reduce the period of milk feeding to 7-10 days, and its quantity to 50-60 kg per animal (Grice et al., 2020; Radchikova et al., 2020).

However, certain requirements shall be met for successful use of whole milk replacers. In terms of nutritional value, they should be equivalent to whole milk, and surpass it in some indicators. One cannot completely replace all components of milk with vegetable ones.

For feeding calves during the entire milk period, it is advisable to use several replacers, depending on the age.

WMR intended for calves up to 30 days of age should contain 40-43% lactose, max. 0.5% fiber, 20-25% protein, with milk protein share of at least 60%.

Advantages of using WMR are also due to as follows:

- they are easy to prepare and easy to dose;
- convenient for transportation and storage (the shelf life is much longer compared to whole milk);
- higher content of vitamins and minerals compared to whole milk.

Until recently, agricultural enterprises used a calf rearing scheme that involves feeding with milk feed for 4 months. However, world practice has proven that milk period can be shortened to 2-3 months. The main criterion for this is physiological development of calves and their ability to consume vegetable feed in the required quantities (Radchikova et al., 2017).

Purpose of the research is to develop a feeding system for calves with the optimal duration of milk period, ensuring normal course of digestion processes, high resistance and productivity of animals during post-milk period.

Research objectives:

- to study chemical composition of feed used for feeding calves during milk and post-milk periods;
- to develop schemes for feeding calves during milk and post-milk periods using whole milk and its replacer, as well as with different duration of milk period;
- to determine intensity of metabolic processes by analyzing morphological and biochemical parameters of blood of experimental animals;
- to determine the effect of the developed feeding schemes for young cattle on indicators of rumen digestion during the post-milk period;
- to study the dynamics of body weight of experimental animals reared using whole milk and its replacers and with different duration of the milk period;
- to determine costs of feed and efficiency of their use for production.

Materials and methods of research

To fulfill the aim set, samples of feed were selected that are used for feeding calves (milk feed, compound feed KR-1, KR-2, grain mixture, silage-and-hay mixture, corn, hay, cereal-and-legume cultures, soybean meal). The analysis of chemical composition of feed was carried out in the laboratory of biochemical analyzes of the Republican Unitary Enterprise Research and Practical Center of the National Academy of Sciences of Belarus for Animal Breeding according to the generally accepted methods of zootechnical analysis. The following was determined in feeds: moisture in accordance with GOST 13496.3-92; calcium, phosphorus (GOST 26570-95; 26657-97); total nitrogen (GOST 13496.4-93), crude fiber (13496.2-91), crude fat (13492.15-97), crude ash (26226-95), dry and organic matter.

To fulfill the aim set, 3 scientific and economic experiments were carried out in conditions of the State Enterprise ZhodinoAgroPlemElita (Table 1).

1. Layout of experiment

Group	Number of animals, animals	Duration of experiment, days	Feeding specification
The first scientific and economic experiment (calves of 10-65 days of age)			
I control	10	55	Main diet (MD) – whole milk, grain mix, hay, compound feed KR-1

II experimental	10	55	MD + WMR
The second scientific and economic experiment (calves of 66-115 days of age)			
I control	10	50	Main diet (MD) – whole milk, corn, silage mixture, compound feed KR-2
II experimental	10	50	MD + DSMR
III experimental	10	50	MD + WMR
The third scientific and economic experiment (calves over 116 days of age)			
I control	10	60	Main diet (MD) – silage mixture, compound feed KR-3
II experimental	10	60	MD
III experimental	10	60	MD

The entire experimental livestock was in the same conditions.

Differences in feeding experimental animals in the 1-2 scientific and economic experiments consisted in the fact that the animals of the control groups received whole milk as part of the diet, and their analogs of the experimental groups were fed with WMR and DSMR.

To determine the physiological state and productivity of experimental young animals during the post-milk period fed with whole milk, WMR, DSMR, the third scientific and economic experiment was carried out.

In the course of the research, zootechnical, biochemical and mathematical methods of analysis were used and the following parameters were studied:

- chemical composition and nutritional value of feed – via samples testing;
- feed consumption – based on the weighing data of the specified feeds and their residues – once every 10 days;
- morphological composition – erythrocytes, leukocytes, hemoglobin, platelets and hematocrit – using MedonicCH620 device (in whole blood); in blood serum: total protein, urea, glucose, phosphorus, calcium, AST, ALT – using ACCENT 200 device, at the end of the experiments, blood from 3 animals from each group was taken to control the physiological state and metabolic processes in their body;
- indicators of rumen digestion by taking rumen fluid from steers bulls in each experimental group. The rumen content was taken through fistula 2-2.5 hours after the morning feeding for two days, and the following was determination in it: values – pH, total nitrogen, ammonia, total volatile fatty acids;
- the growth rate of animals – according to the data of individual weighing of animals at the beginning and at the end of the experiment;
- economic efficiency was determined by the following indicators: the price cost of production, feed cost for obtaining products.

The obtained digital material was processed using method of variation statistics, considering the Student-t validation criteria, using the Microsoft Excel software package.

Results of the research and their discussion

When studying the analyzes of feed chemical composition, it has been determined that the amount of dry matter in hay of cereal grasses used for rearing calves was 850 g and cereal-and-legume mixtures – 890.3 g in 1 kg of natural feed. Content of crude protein in hay of cereal grasses – 71.1 g, of cereals-and-legumes – 96.1 g, crude fat – 15.0 g and 19.8 g, respectively. Crude fiber level in hay of cereal-and-legume grasses was 319.7 g, of cereals – 240.1 g, calcium – 8.21 g and 5.2 g, phosphorus – 3.2 and 2.9 g, respectively.

Studies helped to determine that 1 kg of dry matter of the silage-and-hay mixture contained 426 g, crude protein – 42.0 g, crude fat – 14.3 g, crude fiber – 93.0 g, NFES – 247.2 g, calcium – 3.1 g, and phosphorus – 5.8 g.

Dry matter content in 1 kg of whole milk was 132.7 g, crude protein – 31.3 g, crude fat – 33.9 g, NFES – 45 g, calcium – 1.4 g, and phosphorus – 1.0 g. 1 kg of whole milk replacer contained 945.1 g of dry matter, 226.3 g of crude protein, 107.0 g of crude fat, 13.0 g of calcium and 10.6 g of phosphorus. Content of the basic nutrients in 1 kg of dry skimmed milk replacer was as follows: dry matter – 899.3 g, crude protein – 127.2 g, crude fat – 11.9 g, NFES – 497.3 g, calcium – 12.8 g, and phosphorus – 7.5 g.

In the presented samples, dry matter content in 1 kg of compound feed KR-1, KR-2 and KR-3 was at the level of 885.0-894.0 g, crude protein – 119.1-208.4 g, crude fat – 14.5-30.1 g, crude fiber – 51.1-66.2 g,

NFES – 535.7-658.5 g, crude ash – 26.0-53.6 g, calcium – 7.9-9.4 g, and phosphorus – 4.8-6.1 g.

An experimental whole milk replacer and feeding scheme for calves of 10-65 days of age have been developed for the research.

1 kg of milk product contained 16.6 MJ of metabolizable energy, crude protein – 204 g, crude fat – 162 g, and crude fiber – 14 g.

Feeding with whole milk replacer should be carried out at the correct temperature and at regular intervals (Table 2).

2. Scheme for feeding calves of 10-65 days of age

Calf age	Number of feedings per day x number of liters
day 8	2 x 2 l (75% cow milk/25% WMR)
day 10	2 x 2.5 l (50% cow milk/50% WMR)
day 12	2 x 2.5 l (25% cow milk/75% WMR)
day 13-65	2 x 3 l WMR
from day 14	Concentrated feed, clean water after 0.5-1 hours after feeding with WMR

Note. From 8 to 12 days, the reconstituted WMR was mixed with cow milk.

In the first scientific and economic experiment, whole milk was replaced with a whole milk replacer in diet for calves of the experimental group (Table 3).

3. Average daily diet for experimental animals (based on actually eaten feed)

Feed and nutrients	Group			
	I		II	
	kg	%	kg	%
Compound feed KR-1	0.5	19.8	0.6	24.4
Grain mix	0.2	3.6	0.23	11.0
Whole milk	6.0	69.4	-	-
WMR	-	-	0.75	60.2
Cereal hay	0.2	7.2	0.25	4.4

During the experiment, calves received 1.5-1.5 kg of dry matter in diet. 12.3-13.2 g of digestible protein accounted for 1 kg of metabolizable energy. Concentration of metabolizable energy in 1 kg of dry matter was within the range of 15.5 and 15.2 MJ. Calcium-phosphorus ratio in diets was on the level of 1.34-1.37:1.

Study of morphological and biochemical composition of blood of experimental animals showed (Table 4) that saturation of blood erythrocytes with respiratory pigment - hemoglobin in experimental young animals of group II was 8.7% higher compared to the control analogs, which indicates the intensity of nutrients metabolism. Use of whole milk replacer in diets increased leukocytes count in blood of experimental young animals compared to the control group by 3.0%.

4. Morphological and biochemical composition of blood of calves at the age of 62 days

Parameter	Group	
	I	II
Red blood cells, $10^{12}/L$	7.3 ± 0.5	7.5 ± 0.2
White blood cells, $10^9/L$	6.1 ± 0.4	6.3 ± 0.9
Hemoglobin, g/L	84.2 ± 2.4	91.5 ± 1.2
Total protein, g/L	76.6 ± 0.6	79.1 ± 0.7
Glucose, mmol/L	4.7 ± 0.4	5.2 ± 0.2
Urea, mmol/L	5.3 ± 0.9	4.63 ± 0.9
Platelets, $10^9/L$	463.0 ± 4.7	469.0 ± 5.3
Hematocrit, %	27.8 ± 0.5	29.4 ± 0.2

Notes: * The difference is significant in comparison with the values in the group I of animals, $P < 0.05$.

Studies helped to determine that concentration of glucose in blood increased by 10.6%, respectively, compared to group I, although this indicator was within the physiological standard.

There was also 3.3% increase in the total protein level in blood serum of group II calves and 12.1% decrease in urea in blood, which indicates more efficient use of nitrogen in the body.

The main indicators of calf rearing are body weight and growth rate (Table 5).

5. Variability of body weight and daily average weight gains

Parameter	Group	
	I	II
Body weight:		
- at the beginning of the experiment, kg	39.4 ± 1.5	39.0 ± 1.6
- at the end of the experiment, kg	78.4 ± 2.4	77.1 ± 2.4
Gross weight gain, kg	39.0 ± 2.1	38.1 ± 2.0
Average daily weight gain per experiment, g	709,0 ± 29.6	692,0 ± 38.9
% to control	100.0	97.7

Notes: * The difference is significant in comparison with the values in the group I of animals, P < 0.05.

Results of weighing showed that the average daily weight gain in experimental calves did not differ significantly and amounted to 709 and 692 g. The calves fed with dietary whole milk showed the highest growth energy values, and therefore their gross weight gain during the experiment turned out to be 2.3% higher.

Studies helped to determine that the cost of diet in WMR for experimental steers turned out to be 6.0% cheaper compared to the control group, which affected the price cost of weight gain (Fig. 1).

Inclusion of WMR in the diet for calves of the experimental group II ensured decrease in the cost of weight gain by 3.6% compared to the control group.

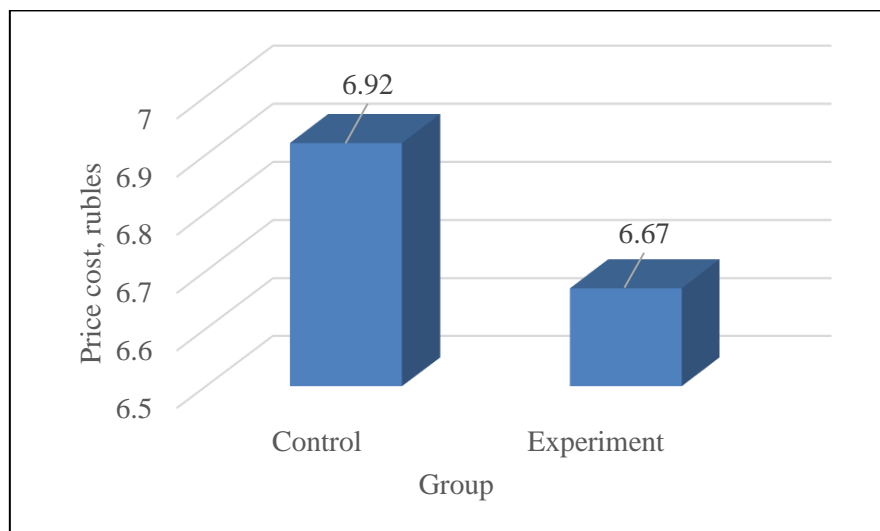


Fig. 1. Price cost of weight gain for obtaining products, rubles.

Thus, the use of whole milk replacer for calves of 10-65 days of age is economically feasible, which is reflected in reduction of price cost for obtaining products.

For research in the second scientific and economic experiment, dry skimmed milk replacer and scheme for feeding calves at the age of 66-115 days were developed (Table 6).

6. Composition and nutritional value of the experimental DSMR for calves

Ingredient, %	DSMR
Dry milk whey	27
Dry skimmed milk	8

Soy meal	28
Wheat meal	7
Dry milk fat concentrate	27
Vitamin and mineral complex	1
1 kg contains:	
Crude protein, g	200
Crude fat, g	157
Fiber, g	13
Metabolizable energy, MJ	16.3

The following was included in DSMR (% wt): dry milk whey – 27, dry skimmed milk – 8, soy meal – 28, wheat meal – 7, dry milk fat concentrate – 27, vitamin and mineral complex – 1.

1 kg of milk product contained: crude protein – 200 g, crude fat – 157 g, fiber – 13 g, metabolic energy – 16.3 MJ.

As a result of control feedings, it has been determined that feed intake by calves during scientific and economic experiment was practically the same (Table 7). Minor differences were noted for the silage-and-hay mixture. The rest of feeds were consumed with no residue.

7. Average daily diet for experimental animals (based on actually eaten feed)

Feed and nutrients	Group		
	I	II	III
Compound feed KR-2, kg	1.0	1.0	1.0
Silage mixture, kg	1.4	1.5	1.5
Whole milk, kg	4.0	-	-
DSMR, kg	-	0.5	-
WMR, kg	-	-	0.5
Corn, kg	0.5	0.5	0.5

The daily diets for experimental calves contained 3.09-3.11 feed units, and concentration in dry matter was at the level of 1.3 feed units. Metabolizable energy concentration in dry matter of diet for experimental animals made 10.95-10.97 MJ. Animals of the control group consumed 12.1 g of digestible protein with feeds, against 13.73 and 13.76 g of consumed by young animals from II and III experimental groups per 1 MJ of metabolizable energy. Energy-protein ratio in the experimental groups made 0.1:1.0.

Consumption of crude fat per 1 kg of dry matter was at the level of 81.9 g in the I control, and 78.2 and 79.3 g – in the II and III experimental groups. Fiber content in 1 kg of dry matter of diet for steers of the I control group was 106.7 g, in the II and III experimental – 113.2 and 114.1 g. Sugar content in dry matter of diet was at the level of 9.9-10.7%.

Calcium-phosphorus ratio in diets was 1.39-1.42:1.

Study of morphological and biochemical composition of blood of experimental animals (Table 8) indicates that inclusion of dry skimmed milk replacer and whole milk replacer in the diet instead of whole milk had no negative effect on physiological state of animals.

8. Morphological and biochemical composition of blood of calves at the age of 113 days

Parameter	Group		
	I	II	III
Red blood cells, $10^{12}/L$	$5,38 \pm 0,40$	$5,34 \pm 0,10$	$5,35 \pm 0,20$
White blood cells, $10^9/L$	$12,70 \pm 0,33$	$9,07 \pm 0,38$	$9,15 \pm 0,46$
Hemoglobin, g/L	123.0 ± 1.7	121.0 ± 2.4	120.0 ± 2.5
Total protein, g/L	46.8 ± 3.4	53.1 ± 2.4	54.0 ± 2.4
Glucose, mmol/L	2.6 ± 0.6	2.8 ± 0.2	2.8 ± 0.3
Urea, mmol/L	4.9 ± 0.1	5.0 ± 0.2	5.1 ± 0.2
Platelets, $10^9/L$	$559,0 \pm 5.4$	$550,0 \pm 5.7$	$555,0 \pm 5.9$
Hematocrit, %	20.5 ± 0.6	20.5 ± 0.7	21.4 ± 0.7
Phosphorus, mmol/L	2.42 ± 0.08	2.82 ± 0.05	2.84 ± 0.05
Calcium, mmol/L	2.08 ± 0.11	2.38 ± 0.14	2.39 ± 0.17

Notes: * The difference is significant in comparison with the values in the control (I) group of animals, $P < 0.05$.

During the experiment, blood indices were recorded to be within physiological standard, which indicates the normal course of metabolic processes in calves of experimental groups.

In blood of young animals of the II and III experimental groups, an increase in concentration of total protein by 13.5 and 15.4%, glucose – 6.5 and 7.3%, calcium – 14.4 and 14.9%, phosphorus – 16.5 and 17.3% had been determined in comparison with control analogues.

Dry skimmed milk replacer and whole milk replacer used instead of whole milk in the diet for calves aged 66-115 days had an insignificant effect on the average daily body weight. So, young animals consuming whole milk reached the average daily weight gain of 982 g, and their coevals from II and III experimental groups 964 and 970 g, respectively. Feed costs per 1 kg of weight gain were recorded to be nearly at the same level (Table 9).

9. Variability of body weight and daily average weight gains

Parameter	Group		
	I	II	III
Body weight at the beginning of the experiment, kg	78.4 ± 2.4	77.1 ± 2.4	77.9 ± 2.5
Body weight at the end of the experiment, kg	127.5 ± 2.7	125.3 ± 2.2	126.4 ± 2.5
Gross weight gain, kg	49.1 ± 1.0	48.2 ± 1.2	48.5 ± 1.4
Average daily weight gain, g	982.0 ± 14.6	964.0 ± 10.7	970.0 ± 11.4
% to control	100.0	98.2	98.8
Feed costs per 1 kg of weight gain, feed units	3.17	3.21	3.20

Notes: * The difference is significant in comparison with the values in the control (I) group of animals, $P < 0.05$.

Analysis of experimental data obtained during scientific and economic experiment indicates that feeding animals with dry skimmed milk replacer in diet contributes to increase in the economic efficiency of rearing young cattle (Fig. 2).

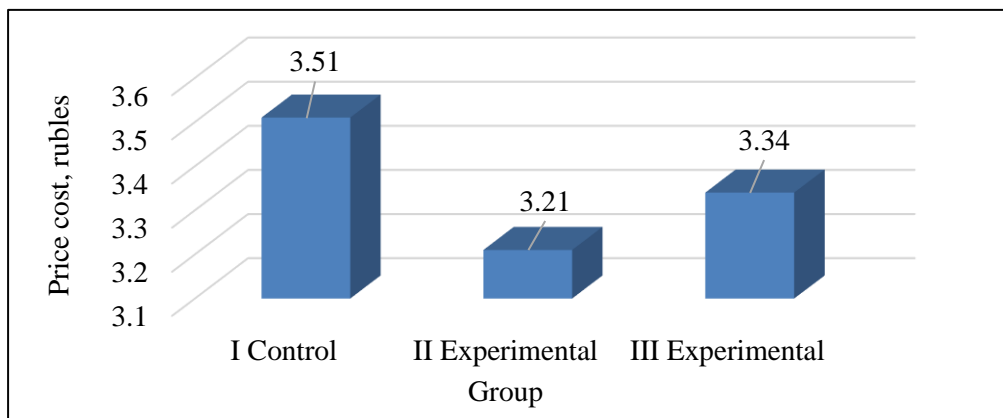


Figure 2 – Price cost of weight gain for obtaining products, rubles.

Cost of daily diet in experimental groups turned to be 10.3 and 5.8% cheaper compared to the control group. Calculation of economic efficiency of use of dry skimmed milk replacer and whole milk replacer by animals in diet showed a decrease in price cost of weight gain by 8.5 and 4.8%.

The main diet for animals for the third experiment was formulated in accordance with the set of feeds available at the farm and used for feeding according to the technology. The diets are formulated according to the main nutrients and presented by the average values for the last two months of the summer period (Table 10).

Succulent feeds in diet made 47.8-50.3%, concentrated feeds – 49.7-52.2%.

Feed consumption records showed that consumption of silage-and-hay mixture in animals of the experimental groups increased by 0.5-0.6 kg.

10. Average daily diet for experimental calves (based on actually eaten feed)

Feed and nutrients	Group					
	I		II		III	
	kg	%	kg	%	kg	%
Compound feed KR-3	1.80	50.3	1.80	47.8	1.80	48.5
Silage mixture	7.0	49.7	7.7	52.2	7.5	51.5

Notes: * The difference is significant in comparison with the values in the control (I) group of animals, $P < 0.05$.

Concentration of metabolizable energy in 1 kg of dry matter made 10.47-10.56 MJ and 0.90-0.91 feed units. Dietary dry matter contained 13.4% of crude protein and 22.4-23.2% of fiber.

Studies helped to determine that all studied blood parameters, reflecting general physiological state of body were within the physiological standard range in the compared groups (Table 11).

11. Morphological and biochemical composition of blood of experimental animals

Parameter	Group		
	I	II	III
Red blood cells, $10^{12}/L$	5.49 ± 0.15	6.04 ± 0.19	6.03 ± 0.17
Hemoglobin, g/L	103.0 ± 2.1	109.0 ± 3.6	107.0 ± 2.9
White blood cells, $10^9/L$	9.57 ± 0.80	9.94 ± 1.10	9.92 ± 1.40
Total protein, g/L	72.9 ± 0.2	72.2 ± 0.1	72.1 ± 0.2
Glucose, mmol/L	3.90 ± 0.19	4.27 ± 0.15	4.29 ± 0.18
Urea, mmol/L	5.45 ± 0.20	5.98 ± 0.22	5.85 ± 0.23
Calcium, mmol/L	2.73 ± 0.05	2.70 ± 0.06	2.69 ± 0.08
Phosphorus, mmol/L	2.85 ± 0.18	3.63 ± 0.16	3.60 ± 0.17
Platelets, $10^9/L$	$329,0 \pm 5.7$	$311,0 \pm 7.6$	$310,0 \pm 7.0$
Hematocrit, %	22.4 ± 0.9	25.7 ± 0.7	24.9 ± 0.8

Notes: * The difference is significant in comparison with the values in the control (I) group of animals, $P < 0.05$.

In the blood of animals of II and III experimental groups, a tendency has been determined to increase concentration of erythrocytes by 10.0 and 9.8%, hemoglobin – by 5.8 and 3.9%, amount of glucose – by 11.0 and 9.5%, respectively, compared to the control. Analysis of the data obtained indicates that metabolic processes in animals of experimental group were more intensive, which influenced productivity of young stock.

Study of growth dynamics of experimental animals for the reporting period of the scientific and economic experiment showed that increase in body weight of young animals in the experimental groups was more intensive compared to the control (Table 12).

12. Dynamics of body weight and daily average weight gains

Parameter	Group		
	I	II	III
Body weight, kg: at the beginning of the experiment	127.5 ± 5.3	125.3 ± 5.36	126.4 ± 5.7
at the end of the experiment	175.3 ± 8.0	177.5 ± 8.2	179.3 ± 8.4
Gross weight gain, kg	47.8 ± 3.5	52.2 ± 5.0	52.9 ± 5.0
Average daily weight gain per experiment, g	$797,0 \pm 47.6$	$870,0 \pm 43.3$	$882,0 \pm 49.1$
% to control	100.0 ± 1.0	$109.2 \pm 0.5^*$	$110.7 \pm 0.9^*$
Feed costs per 1 kg of weight gain, feed units	5.12	4.93	4.80

Notes: * The difference is significant in comparison with the values in the control (I) group of animals, $P < 0.05$.

At the same time, the average daily weight gain of calves in the control group made 797 g, and in the experimental group – 870,0 and 882,0 g. The average daily weight gain in young animals

of the II and III experimental groups was 9.2 and 10.7% higher ($P < 0.05$). Increase in the growth energy of steers of the experimental group made it possible to obtain additional 4.4 and 5.1 kg of body weight per animal.

As a result of increase in productivity of animals of the experimental groups, feed costs for obtaining products decreased by 3.7 and 6.3% and amounted to 4.93 and 4.80 feed units per 1 kg of weight gain.

Based on the results obtained, it has been determined that cost of feed per 1 kg of weight gain in the II and III experimental groups was 5.8 and 7.6% lower compared to the control, which influenced decrease in the cost of weight gain (Fig. 3).

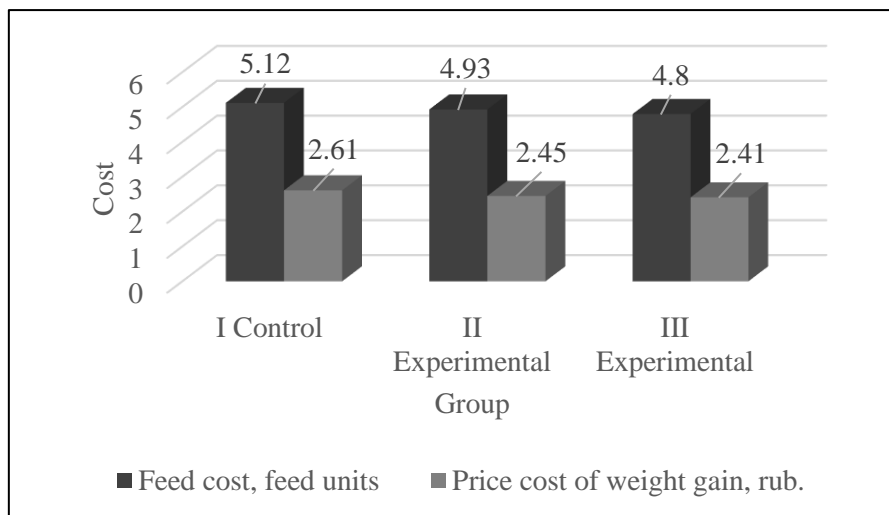


Fig. 3. Feed cost and price cost of weight gain for obtaining products, rubles

Price cost of weight gain in experimental groups compared to the control analogs decreased by 6.1 and 7.7%. It allowed to obtain additional profit in the experimental groups in the amount of 8.35 (3.5 USD) and 10.58 (4.5 USD) rubles per animal during the research period.

Conclusions and perspectives

Based on the research conducted, it has been determined that feeding calves with experimental milk replacer with milk period duration of 65 days allowed to obtain 692,0 g of the average daily weight gain for the experiment period, that is 2.3% lower than the control indicator. Feeding calves with WMR helps to reduce the cost of diet by 6.0% and the price cost of weight gain by 3.6%. Use of dry skimmed milk replacer and whole milk replacer during the rearing period, with milk period duration of 115 days, contributed to decrease in weight gain by 1.8 and 1.2% compared to the control variant. Feeding calves with DSMR and WMR helped to reduce the cost of diet by 10.3 and 5.8% and the price cost of weight gain by 8.5 and 4.8%. It has been determined that DSMR and WMR in diet for young animals over 115 days of age during the post-milk period increases concentration of erythrocytes in blood by 10.0 and 9.8%, hemoglobin – by 5.8 and 3.9%, amount of glucose – by 11.0 and 9.5%. Inclusion of DSMR and WMR in diet for young cattle with milk period duration of 65 and 115 days contributed to increase in the average daily weight gain in the post-milk period by 9.2 and 10.7%, while reducing the cost of feed by 5.8 and 7.6%, price cost of weight gain by 6.1 and 7.7% and increase in additional profit in the amount of 8.35 (3.5 USD) and 10.58 (4.5 USD) rubles per animal during experimental period.

In the future, it is necessary to improve the feeding system of young cattle using new developments in this area.

References

Antonovich, A. M., & Dolzenkova, E. A. (2019). Granulated high-protein feed as part of the KR-3 compound feed for young cattle. Scientific notes of the educational institution Vitebsk Order of the Badge of Honor State Academy of Veterinary Medicine, 55(3), 108-112 (in Russian).

Boorboor, M., Alamouti, A. A., Karimi, N., & Belverdy, M. S (2020). Effects of reducing crude protein concentration in starter feed containing constant rumen undegradable protein on dairy calves

- performance. *Journal of Animal Physiology and Animal Nutrition*, 104(5), 1287-1293. doi: [10.1111/jpn.13380](https://doi.org/10.1111/jpn.13380).
- Buryakov, N. P., Buryakova, M. A., Suslova, I. A., Zaikina, A. S., Aleshin, D. E., & Stavtcev, A. E. (2019). Influence of protein concentrate in the diet on productivity and amino acid composition of cow milk. *IOP Conference series: Earth and Environmental Science*, 341, 012057. doi: [10.1088/1755-1315/341/1/012057](https://doi.org/10.1088/1755-1315/341/1/012057)
- Dalla Martha, G. O., D'Oliveira, M. C., Vedovatto, M., Cortada Neto, I. M., Franco, G. L., & Diogo, J. M. S. (2020). Calves performance after the inclusion of slow-release urea in protein supplement for beef cattle. *Archivos de Zootecnia*, 69(266), 208-214.
- Dolzenkova, E. A., & Yatzko N. A. (2016). Cicatricial digestion, metabolism, feed conversion when feeding Kryptolife-S feed additive to bull calves. *Zootechnical Science of Belarus*, 51(1), 274-286 (in Russian). doi: [10.32845/bsnau.lvst.2021.2.21](https://doi.org/10.32845/bsnau.lvst.2021.2.21)
- Gading, B. M. W. T., Agus, A., Irawan, A., & Panjono, P. (2020). Growth performance, hematological and mineral profile of post-weaning calves as influenced by inclusion of pelleted-concentrate supplement containing essential oils and probiotics. *Iranian Journal of Applied Animal Science*, 10(3), 461-468 (http://www.iaujournals.ir/article_675343_885d26155ceb8c4190bf285af6c538b6.pdf)
- Grice, K. D., Glosson, K. M., & Drackley, J. K. (2020). Effects of feeding frequency and protein source in milk replacer for Holstein calves. *Journal of Dairy Science*, 103(11), 10048-10059. doi: [10.3168/jds.2020-19041](https://doi.org/10.3168/jds.2020-19041)
- Jiang, X., Xu, H. J., Cui, Z. Q., & Zhang, Y. G. (2020). Effects of supplementation with *Lactobacillus plantarum* 299v on the performance, blood metabolites, rumen fermentation and bacterial communities of preweaning calves. *Livestock Science*; 239 Amsterdam: Elsevier B. V. doi: [10.1016/j.livsci.2020.104120](https://doi.org/10.1016/j.livsci.2020.104120)
- Liu, Ting, Hultquist, K., Froehlich, K., & Casper, D. P. (2020). Feeding an amino acid-formulated milk replacer for Holstein calves during 2 time periods. *Journal of Dairy Science*, 10 (11), 10108-10121 doi: [10.3168/jds.2020-18529](https://doi.org/10.3168/jds.2020-18529).
- Lopez, A. J., Jones, C. M., Geiger, A. J., & Heinrichs, A. J. (2020). Variation in serum immunoglobulin G concentrations from birth to 112 days of age in Holstein calves fed a commercial colostrum replacer or maternal colostrum. *Journal of Dairy Science*; 103(8), Philadelphia: Elsevier Inc.; 7535-7539. doi: [10.3168/jds.2020-18400](https://doi.org/10.3168/jds.2020-18400)
- Marques, R. S., Bohnert, D. W., Sousa de, O. A., Brandão, A. P., Schumacher, T. F., Schubach, K. M., Vilela, M. P., Rett, B., & Cooke, R. F. (2019). Impact of 24-h feed, water, or feed and water deprivation on feed intake, metabolic, and inflammatory responses in beef heifers. *Journal of Animal Science*, 97(1), 398-406. doi: [10.1093/jas/sky397](https://doi.org/10.1093/jas/sky397)
- Radchikova, G. N., Kot, A. N., Medvedsky, V. A., Shareiko, N. A., Ganushchenko, O. F., Vozmitel, L. A., Karelin, V. V., Bukas, V. V., & Kurtina, V. N. (2018). Compound feed KR-2 with inclusion of dry skimmed milk replacer in diets for calves. *Zootechnical Science of Belarus*, 53(2), 75-83 (in Russian).
- Radchikova, G. N., Pilyuk, S. N., Serguchev, S. V., Kot, A. N., Vozmitel, L. A., Broshkov, M. M., Danchuk, A. V., Stoyanovskiy, V. G., & Darmogray, L. M. (2020). Efficiency of using WMR with different level of milk sugar in compound feed KR-2 for young cattle. *Sore issues of improving quality and safety of production and processing of agricultural products. Materials of the International Scientific and Practical Conference. Dnipro State Agrarian and Economic University, Institute of Grain Crops of the National Academy of Sciences of Ukraine*, 63-65 (in Russian).
- Radchikova, G. N., Sapsaleva, T. L., Lyundyshev, V. A., Shareiko, N. A., Vozmitel, L. A., Karelin, V. V., Bukas, V. V., Radko, M. E., Lemeshevsky, V. O., & Yanochkin, I. V. (2020). Use of WMR for young cattle of 10-65 days of age. *Zootechnical Science of Belarus*, 55(2), 96-105 (in Russian).
- Radchikova, G. N., Vozmitel, L. A., Suchkova, I. V., Stoyanovskiy, V. G., Pivtorak, Y. I., Broshkov, M. M., Zinoviev, S. G., Trokoz, V. A., Karpovsky, V. I., & Pentilyuk, S. I. (2017). Efficiency of feeding with whole milk replacers with different protein level in diets for calves. *Zootechnical Science of Belarus*. 52(2), 26-34 (in Russian).
- Rai, S., Mandal, S., Behera, R., Sahu, J., Dutta, T. K., Jas, R., Chatterjee, A., Mandal, D. K., Karunakaran, M., & Ghosh, M. K. (2020). Effect of feeding fermentable synbiotics (*Lactobacillus rhamnosus* NCDC 298 and fructo-oligosaccharide) to Jersey crossbred calves up to 3 months of age. *Indian Journal of Animal Sciences*, 90(4), New Delhi: Indian Council of Agricultural Research, 614-617.
- Sintzerova, A. M., & Zalnerovskaya, A. V. (2019). The feed additive BVMD "Premium-2" in the diets of calves. *Scientific Notes of the educational institution Vitebsk Order of the Badge of Honor State Academy of Veterinary Medicine*, 55(3), 151-154 (in Russian).

Smynev, V. I., Motyzko, N. S., Lapotentov, A. M., Razymovski, N. I., Ganyshenko, O. F., & Matzinovich, A. A. (2017). Technology of obtaining and growing healthy calves: monograph, Vitebsk (in Russian).

Shiasi Sardoabi, R., Alikhani, M., Hashemzadeh, F., Khorvash, M., Mirzaei, M., & Drackley, J. K. (2021). Effects of different planes of milk feeding and milk total solids concentration on growth, ruminal fermentation, health, and behavior of late weaned dairy calves during summer. *Journal of Animal Science and Biotechnology*, 12, 96. doi:10.1186/s40104-021-00615-w

Turini, L., Conte, G., Bonelli, F., Sgorbini, M., Madrigali, A., & Mele, M. (2020). The relationship between colostrum quality, passive transfer of immunity and birth and weaning weight in neonatal calves. *Livestock Science*; 238 Amsterdam: Elsevier B.V. doi: [10.1016/j.livsci.2020.104033](https://doi.org/10.1016/j.livsci.2020.104033)

Радчиков В. Ф., Богданович, Д. М. Кот А. Н., Цай В. П., Томчук В. А., Грищенко В. А., Карповський В. І., Трокоз В. О. (2021). Сучасна система вирощування телят. Ukrainian Journal of Veterinary Sciences. Вирощування телят має вирішальне значення для успішного молочного або м'ясного скотарства. Тільки від здорових телят можна отримати максимальну продуктивність при найменших витратах.

При проведенні дослідів використовували зоотехнічні, біохімічні, економічні методи досліджень.

Встановлено, що згодовування дослідного замітника незбираного молока (ЗНМ) телятам з тривалістю молочного періоду 65 діб дозволило отримати за період досліду 692 г середньодобового приросту, що на 2,3% нижче контрольного показника. Випоювання телятам ЗНМ дозволяє знизити вартість раціону на 6,0% і собівартість приросту на 3,6%.

Використання замітника сухого знежиреного молока і ЗНМ в період вирощування молодняку (молочний період – 115 діб) знижує приріст маси тіла лише на 1,8 і 1,2% порівняно з контролем із одночасним зниженням вартості раціону на 10,3 і 5,8% і собівартості приросту на 8,5 і 4,8%.

Згодовування сухого знежиреного молока і ЗНМ у складі раціону молодняку старше 115 діб в післямолочний період сприяє підвищенню в крові кількості еритроцитів на 10,0 і 9,8 і вмісту гемоглобіну – 5,8 і 3,9 та глюкози – 11,0 і 9,5% відповідно.

Включення в раціон молодняку великої рогатої худоби незбираного та сухого знежиреного молока, з тривалістю молочного періоду 65 і 115 діб підвищує середньодобовий приріст у післямолочний період на 9,2 і 10,7%, при зниженні вартості кормів на 5,8 і 7,6%, собівартості приросту – 6,1 і 7,7% і збільшення додаткового прибутку в розмірі 8,35 і 10,58 рублів (3,5 і 4,5 доларів США) на голову за період досліджень.

Надалі необхідно вдосконалювати систему годівлі молодняку великої рогатої худоби з використанням нових розробок у цій галузі.

Ключові слова: молодняк великої рогатої худоби, незбиране молоко, замітник незбираного молока, замітник сухого знежиреного молока, гематологічні показники, продуктивність, ефективність.

QUALITY OF RAW MILK AND ITS FATTY ACID COMPOSITION

O. M. IAKUBCHAK¹, Doctor of Veterinary Sciences, Professor
<https://orcid.org/0000-0002-9390-6578>

T. V. TARAN¹, PhD, associated professor,
<https://orcid.org/0000-0002-9370-8539>

S. V. MIDYK², PhD, Head of the research department for monitoring the safety of agricultural products
<http://orcid.org/0000-0002-2682-2884>

V. V. DANCHUK², Doctor of Agricultural Sciences, Professor,
<https://orcid.org/0000-0003-2156-1758>

N. YA. DUDCHENKO¹, Head of the Research Department for Monitoring the Product Quality of
Agroindustrial Complex,
<http://orcid.org/0000-0002-8283-5305>

L. M. VYGOVSKA², Doctor of Veterinary Sciences, Head of the Department of Microbiological Research,
<https://orcid.org/0000-0001-6745-5753>

¹Department of Veterinary Hygiene named after Professor A.K. Skorokhodko

²Ukrainian Laboratory of Quality and Safety of Agricultural Products

National University of Life and Environmental Sciences of Ukraine

E-mail: olga.yakubchak@gmail.com; ttaran@ukr.net; svit.mid@gmail.com

Abstract. *The study of the influence of the season on the organoleptic and physicochemical parameters of milk is still relevant. In addition, the ratio of fatty acids in the milk of cows characterizes the level of their feeding and the study of these indicators is relevant given the prevalence of adulteration of milk and dairy products with vegetable oils. The aim was to study individual indicators of raw milk quality depending on the season and its fatty acid composition.*

*The material for the study was prefabricated chilled raw milk obtained at different times of the year on the dairy farm of NULES of Ukraine "Agronomic Research Station". The research was conducted in the accredited Ukrainian Laboratory of Quality and Safety of AIC NULES of Ukraine. Organoleptic, physicochemical, sanitary and hygienic were determined by generally accepted standard methods. The fatty acid composition of milk was investigated by gas chromatography. Extraction of lipids from milk was performed by the method of Folch. Analysis of LCD methyl esters was performed on a Trace GC Ultra gas chromatograph (USA) with a flame ionization detector. Identification of fatty acids was performed using a standard sample Supelco 37 Component FAME Mix. Quantitative evaluation of the fatty acid spectrum of milk fat lipids was performed by the method of internal normalization with their determination in percent. The study was performed in 2 parallels. Statistical processing of experimental data was performed by conventional methods of variation statistics. The probability of the difference in indicators was assessed by Student's *t*-test. Differences between the compared indicators were considered significant at the significance level $P < 0.05$. Studies have shown that milk organoleptic and physicochemical parameters of raw milk vary depending on the season. In terms of microbiological indicators, the milk corresponded to the first grade, although in winter, according to other indicators, it could be attributed to the extra, or at worst, to the highest grade. In addition, in winter the content of saturated fatty acids in milk increases. The content of unsaturated fatty acids increases in summer and autumn due to the presence of green mass and corn silage in the diet of cows. The obtained results can be used as a basis for preparing a diet to obtain milk with optimal content and ratio of fatty acids, which can become competitive in the market of raw milk to produce milk and dairy products of improved chemical composition, dietary, functional products, baby food.*

Key words: raw milk, quality, sanitary and hygienic indicators, fatty acids

Introduction. Milk and dairy products always play an important role in people's diet. They are an indispensable source of energy, and it is scientifically substantiated that dairy products should make up a third of the caloric content of a person's daily diet. Importance belongs to the dietary properties of milk fat, 95% of which are triglycerides more than 40% of fatty acids (trans-isomers of unsaturated fatty acids, short chain acids with an odd number of carbon atoms and a branched chain, which are synthesized by the ruminant microflora (Magan et al., 2021).

Analysis of recent research and publications. The ratio of fatty acids in milk fat depends on the composition of the diet of animals and can vary widely. It is known that the highest content of unsaturated fatty acids in milk fat, as well as diene conjugates of linoleic acid is observed in the grazing period

(Yamaguchi et al., 2017; Bainbridge et al., 2017). This is since green foods contain a significant amount of their precursors - polyunsaturated fatty acids. During the stall period, the proportion of saturated fatty acids increases and diene conjugates of linoleic acid decrease (Pegolo et al., 2017).

If a high-concentration diet with a low fiber content in milk fat is used, the content of trans-isomers of acid increases by 18:1 due to incomplete biohydrogenation of linolenic and linoleic acids by the rumen microflora. If the ratio of roughage to concentrates is changed from 50:50 to 20:80, the total amount of scarring and vaccine acids in milk is halved. Also, the fatty acid composition of milk fat is influenced by the breed of cows, pregnancy, etc. (Barreiro et al., 2017) and the method of technological processing of feed (Oliveira et al., 2021; Lanza et al., 2021).

The organoleptic parameters and features of the technological properties of milk are influenced by the fatty acid composition of milk fat, because it depends on the intensity of the oxidation process. Regarding the content of biologically active compounds in milk and dairy products, which are more important for the consumer, they include: branched fatty acids and diene conjugates of linoleic acid, essential fatty acids, butyric acid. However, there are also potentially dangerous to human health fatty acids (myristic, palmitic, lauric).

A significant amount of research is devoted to the characteristics of the fatty acid composition of milk fat (Silva et al., 2018; Dias et al., 2019; Musayeva et al., 2021).

Currently, several regulations on milk safety and quality have been harmonized in Ukraine. In particular, according to Order 118 of 12.03.2019 "Requirements for safety and quality of milk and dairy products" (Ministry of Agrarian Policy and Food, 2019), requirements are set for market operators that implement good practices of production, processing and marketing of milk and dairy products. , establish criteria for raw milk, among which the main ones are microbiological and somatic cell content (Yakubchak, et al. 2021), which are important for suitability for introduction into circulation of milk. Milk is also tested for mycotoxins in both Ukraine and the EU (Yakubchak et al., 2018). The maximum permissible concentrations of individual mycotoxins are regulated by the relevant regulations (Commission Regulation (EU) № 165/2010, 2010; Nakaz MON № 368, 2013).

Among the main indicators of milk quality in the current regulations there is no information on such biologically active components as fatty acids, which can fluctuate significantly at different times of the year. Given that humanity is trying to pay more attention to healthy eating, the creation of functional products (Pu et al., 2021; Prosser, 2021), it is important to study the fatty acid composition of milk obtained in small farms, which are now the main raw material base for capacity for the production of milk and dairy products in Ukraine. In particular, one of such farms is a separate subdivision of the National University of Life and Environmental Sciences of Ukraine "Agronomic Research Station" (SE NULES of Ukraine "Agronomic Research Station").

Given this, **the aim of our work** was to study individual quality indicators of raw milk depending on the season and its fatty acid composition.

Materials and methods of research. The milk obtained from the NUBIP of Ukraine "Agronomic Research Station" was studied. Samples were taken from whole cooling milk, respectively (DSTU ISO 707: 2002, 2002; DSTU 8553: 2015, 2015). Milk was obtained from cows of the black-spotted family with tethered keeping at different times of the year. On the farm, as a supplement - mechanical, profitable equipment of the companies "Bratslav", giving three approvals, in spring and summer; twice - in the fall. The research was conducted based on ULYABP AIC NULES of Ukraine.

Organoleptic parameters were determined: appearance, color, taste, smell, consistency. Density, mass fraction of fat, protein, and lactose were determined by ultrasound on a Master Classis LM2PI milk analyzer. The same device, in addition, determined: active acidity, dry skim milk residue, freezing point, electrical conductivity, mass fraction of minerals, mass fraction of water, freezing point.

Extraction of lipids from milk was performed by the method of Folch (Folch, 1957). The next step in sample preparation was to hydrolyze and methylate fatty acids of lipids obtained from pooled milk samples. To do this, 4 cm³ of methyl sodium hydroxide solution was added to 100 mg of the obtained fat, the reflux condenser was connected to the flask containing it and boiled until the fat droplets disappeared, stirring the contents of the flask at intervals of 30-60 seconds. To the contents of the flask was added 5 cm³ of methyl boron trifluoride solution, continuing to boil for up to 1 hour. 3 cm³ of hexane was added to the boiling mixture through the top of the reflux condenser and removed from the heating element. To a still hot solution was added 20 cm³ of saturated sodium chloride solution and stirred for 15 sec. The top (hexane) layer was selected for the study according to the current DSTU (DSTU ISO 5509-2002, 2002). Analysis of LCD methyl esters was performed on a Trace GC Ultra gas chromatograph (USA) with a flame ionization detector. Chromatography conditions: column temperature 140-240 °C, detector temperature - 260 °C. The sample was introduced into the chromatograph using a TriPlus autosampler at a dose of 1 µl. The duration of the analysis was 65 minutes

Identification of fatty acids was performed using a standard sample Supelco 37 Component FAME Mix. Quantitative evaluation of the fatty acid spectrum of milk fat lipids was performed by the method of internal normalization, determining their content in percent. The studies were performed in 2 parallels according to the current DSTU (DSTU ISO 5508: 2001, 2001).

Statistical processing of experimental data was performed by conventional methods of variation statistics. The probability of the difference in indicators was assessed by Student's t-test. Differences between the compared indicators were considered significant at the significance level $P < 0.05$.

Results of the study and their discussion. The first stage of our work was the analysis of the fodder base on the farm of NULES of Ukraine "Agronomic Research Station" depending on the season (Table 1).

1. A set of feeds for the formation of the diet, depending on the season.

List of feeds	Seasons			
	winter	spring	summer	autumn
Concentrated feed: corn; barley; wheat; sunflower cake	+	+	+	+
Vitamin and mineral supplements: "Calcium" firm "Vita" (calcium, magnesium, phosphorus, sodium chloride); common salt; Molasses	+	+	+	+
Green table (alfalfa)	-	+	+	+
Corn silage. withinage (alfalfa); cino (alfalfa); witholoma (achminna)	-	+	+	+

Data Table. 1 indicate that in the diet of cows throughout the year there are concentrated feeds and vitamin and mineral supplements: "Calcium" company "Vita" (calcium, magnesium, phosphorus, sodium chloride); common salt; molasses. Green mass in the diet is from mid-April to late September. Corn silage; haylage (alfalfa); hay (alfalfa); straw (barley) is present in the diet of cows in spring, summer and autumn, and absent - in winter.

According to organoleptic parameters, milk in all seasons of the year complied with current regulations and had the following characteristics. Consistency - a homogeneous liquid without flakes of protein and sediment; taste and smell are pure, inherent in fresh milk, without extraneous tastes and smells; color - from white to light cream. From May to the end of September, raw milk has a pronounced yellowish tinge.

Physico-chemical and sanitary-hygienic parameters of milk were also compared, depending on the season and the diet of animals (Tables 2, 3).

2. Results of physical and chemical studies of cow's milk obtained in the conditions of THE NUBIP of Ukraine "Agronomic Research Station", $M \pm m$, $n=16$

Name of indicators, units of measurement	Winter	Spring	Summer	Autumn	Norms according to the ND ¹		
					extra	higher	first
Mass fraction of solids, %	12,92 ± 0,10	12,4 ± 0,11*	12,35 ± 0,09**	12,62 ± 0,18	≥ 12,0	≥ 11,8	≥ 11,5
Mass fraction of fat, %	3,78 ± 0,29	3,41 ± 0,56	3,33 ± 0,12*	3,57 ± 0,11	≥ 3,2 %		

Density, кг/м ³	1031 ± 1,10	1030 ± 1,43	10,31 ± 1,32	1031 ± 1,87	1028,0	not less than 1027,0	
Mass fraction of protein, %	3,42 ± 0,76	3,37 ± 0,11	3,32 ± 0,64	3,38 ± 0,32	≥ 2,8%		
Mass fraction of lactose, %	5,13 ± 0,28	5,05 ± 0,30	4,09 ± 0,36*	5,07 ± 0,62	is not normalized		
Mass fraction of minerals, %	0,76 ± 0,04	0,75 ± 0,06	0,75 ± 0,02	0,71 ± 0,06	is not normalized		
Mass fraction of water, %	0,00	0,00	0,00	0,00	is not normalized		
Freezing point, (minus) °C	0,592 ± 0,07	0,587 ± 0,03	0,589 ± 0,02	0,590 ± 0,06	not higher than minus 0,520		
Electroconductivity, mS/cm	5,0 ± 0,11	5,1 ± 0,32	5,1 ± 0,21	5,2 ± 0,11	is not normalized		
Active kislotn, from. pH	6,94 ± 0,11	6,90 ± 0,78	6,86 ± 0,84	6,73 ± 0,05*	from 6,6 до 6,7		from 6,55 before 6,8
Titric acidity, °T	17 ± 0,5	18 ± 0,3	19 ± 0,1**	18 ± 0,2	16–17	16–18	16–19
Milk temperature, °C, not higher than	6	6	7	6	8	8	8
Group of cleanliness, not lower than	I	I	I	I	I		

Note: * P < 0,05, ** P < 0,01, ND¹ – Determination of milk quality indicators: DSTU 7057: 2009 Raw cow's milk. Ultrasonic determination of density, mass fraction of fat, protein, dry matter and lactose. DSTU 3662: 2018 Milk is raw cow. Specifications.

According to the complex of physicochemical parameters (Table 2): mass fraction of dry matter, density, titrated acidity, purity group, freezing point, temperature of milk obtained in the conditions of NULES of Ukraine "Agronomic Research Station" corresponded to the first grade. All studied indicators corresponded to the current standard. However, it should be noted that the mass fraction of dry matter, density, purity group, freezing point, temperature, milk corresponded to the extra grade. However, the worst indicator was the titratable acidity index, according to which the first grade was exhibited. Titrated acidity of milk is a sanitary and hygienic indicator of its production, which indicates non-compliance with hygienic requirements for obtaining milk of proper quality on this farm.

Other indicators that are normalized but do not affect the grade also met the requirements of current regulations (DSTU 3662: 2018, 2018). The mass fraction of fat and protein was lowest in summer and highest in winter, which can be explained by the predominance in the diet of green cows in summer and concentrated and dry feed in winter.

Although the mass fraction of lactose in Ukraine is not regulated, it is an important indicator of milk quality and regulated by European legislation, it is especially important to produce dairy products for baby food. This figure was lowest in summer, and at other times of the year almost at the same level, and in general was quite high. Mass fraction of minerals, electrical conductivity and active acidity did not differ statistically, depending on the season.

3. Results of the study of sanitary and hygienic indicators of milk, M±m, n=16

Name of indicators, units of measurement	Winter	Spring	Summer	Autumn	Norms according to the ND*		
					extra	higher	first

Number of mesophilic aerobic and optional anaerobic microorganisms* (KMAFANM for temperatures 30 ^C), ted. KUO/cm ³	476,31 ± 1,06	489,12 ± 3,7*	331,27 ± 1,13**	427,02 ± 2,21**	≤ 100	≤ 300	≤ 500
Number of somatic cells*, thousand/cm ³	486,31 ± 28,02	463,13 ± 21,01	378,41 ± 23,03*	425,14 ± 18,02	≤ 400	≤ 400	≤ 500
In the appearance of bacteria of the group of intestinal sticks, the presence of 1 cm ³	< 3	< 3	< 4	< 4	< 3	< 3	< 3
In the appearance of pathogenic microorganisms, including bacteria of the genus <i>Salmonella</i> , 25 cm ³	–	–	–	–	не дозволено	не дозволено	не дозволено
Detection of coagulase-positive <i>Staphylococcus aureus</i> , in 1 cm ³	–	–	–	–	не дозволено	не дозволено	не дозволено

Note: *P < 0.05, **P < 0.001. Indicators were determined by the variable geometric mean of the relevant monthly analyzes for a certain period: the content of microorganisms - for a two-month period, on samples that are taken at least twice a month; somatic cell content - for a three-month period, at least one sample per month.

According to the hygienic indicators of KMAFANM and the number of somatic cells, the milk corresponded to the first grade, except for the number of somatic cells and the summer period, mother's milk according to this indicator could be attributed to the highest grade. For other microbiological parameters that do not affect the grade of milk, bacteria of the *Escherichia coli* group in 1 cm³ were higher than normal in summer and autumn. Pathogenic microorganisms, including bacteria of the genus *Salmonella*, in 25 cm³ and coagulase-positive *Staphylococcus aureus*, in 1 cm³ was not found to meet the requirements of current regulations.

Milk of different species is characterized by a specific fatty acid composition. It is known that cow's milk is also characterized by a certain content of fatty acids. The species identification of milk can be determined by the fatty acid composition, which can fluctuate slightly, but is relatively stable. Significant changes in the fatty acid content may indicate milk from mastitis in cows or its adulteration (replacement of milk fat with non-dairy) (Paredes et al, 2018).

Therefore, the next stage of our work was the study of the fatty acid composition of milk. By gas chromatography, 17 fatty acids were identified in milk-raw samples (Table 4).

Depending on the time of year (the effect of the diet), the content of individual fatty acids changed.

4. Fatty acid composition of cow's milk, obtained in the conditions of the NUBIP of Ukraine "Agronomic Research Station", M ± m, n = 16

Name and code of fatty acid	Winter	Spring	Autumn	Summer	*Norm by ND
Butyric acid (C4:0)	3,65 ± 0,16	2,84 ± 0,13**	3,84 ± 0,18	2,90 ± 0,23*	2.0-4.5
Capronic acid (C6:0)	2,78 ± 0,10	2,17 ± 0,11**	2,57 ± 0,22	1,87 ± 0,09***	1.5-3.0
Caprylic acid (C8:0)	1,70 ± 0,08	1,21 ± 0,06**	1,61 ± 0,04	1,54 ± 0,14	1.0-2.0
Capric acid (C10:0)	3,41 ± 0,21	2,77 ± 0,08*	3,17 ± 0,07	2,54 ± 0,02**	2.0-3.5
Lauric acid (C12:0)	3,54 ± 0,12	3,12 ± 0,11*	3,32 ± 0,06	3,18 ± 0,14	2.0-4.0
Miristinova acid (C14:0)	11,60 ± 1,84	10,74 ± 0,56	12,74 ± 0,64	10,03 ± 0,60	8.0-13.0

Miristinoleinova acid(C14:1)	0,79 ± 0,06	1,18 ± 0,09**	1,20 ± 0,08*	1,23 ± 0,11**	0.6-1.5
Pentadecanic acid (C15:0)	1,96 ± 0,11	1,23 ± 0,06***	1,87 ± 0,32	1,80 ± 0,05	3.0-4.5
Palmitic acid (C16:0)	28,83 ± 2,65	28,17 ± 0,95	22,17 ± 1,1*	26,17 ± 1,08	22.0-33.0
Palmatinoleic acid (C16:1)	1,87 ± 0,09	1,90 ± 0,06	1,87 ± 0,07	1,93 ± 0,13	1.5-2.0
Heptadecanic acid (C17:0)	0,87±0,04	0,85 ± 0,05	0,80 ± 0,11	0,80 ± 0,10	2.0.-4.0
Stearic acidC18:0	12,11±0,87	11,90 ± 1,43	10,62 ± 1,12	10,11 ± 1,07	9.0-13.0
Oleic acid (C18:1ω9c)	22,62 ± 1,98	26,94 ± 1.12	28,74 ± 2,78	31,05 ± 2,35*	22.0-32.0
Lynolev acid (C18:2ω6c)	3,76 ± 0,32	4,48 ± 0,11	4,86 ± 0,16	4,22 ± 0,2	3.0-5.5
Arachic acid (C20:0)	0,16 ± 0,06	0,12 ± 0,04	0,15 ± 0,03	0,13 ± 0,02	до 0.3
Tinolenic acid (C18:3ω3)	0,27 ± 0,09	0,30 ± 0,07	0,41 ± 0,05	0,44 ± 0,03	до 1.5
Begenic acid (C22:0)	0,08 ± 0,02	0,08 ± 0,02	0,06 ± 0,02	0,06 ± 0,02	до 0.1

Note: *P < 0.05, ** P < 0.01, ***P < 0.001. Interstate standard GOST 52253-2004 Butter and butter paste from cow's milk. General technical conditions (with change №1) (Butter and butter paste from cow's milk. General technical conditions (with changes №1)). Valid, but does not operate in Ukraine. Interstate standard GOST 52253-2004 Butter and butter paste from cow's milk. General technical conditions (with change №1) (Butter and butter paste from cow's milk. General technical conditions (with changes №1)).

As can be seen from the data presented in table. 3, milk fat differs in the ratio of fatty acids depending on the season and feeding of cows.

The content of saturated fatty acids in the experimental milk was mostly normal. In winter and autumn, a higher content of butyric, kapron, caprylic, capric, lauric, myristic, pentadecanoic and other saturated fatty acids was noted. Milk of all seasons showed a slightly lower content compared to the normative indicators of pentadecanoic (C15: 0) and heptadecanoic (C17: 0) fatty acids.

Unsaturated fatty acids myristic and palmitic in milk were also within normal limits and their number varied according to the seasons. The content of myristic acid was higher in summer and palmitic was stable throughout the year, oleic acid ω 9 predominated in autumn and summer milk, linoleic acid ω 6 predominated in autumn and spring milk, linolenic ω 3 - in autumn and summer when present in the diet. feed and silage.

It should be noted that the amount of saturated fatty acids (SFA) in the studied raw milk in the winter increases by 9.56% compared to summer milk. Monounsaturated fatty acids are contained in summer milk by 8.93% more than in winter. Polyunsaturated fatty acids, including ω 3, are most abundant in summer and autumn milk (Fig. 1).

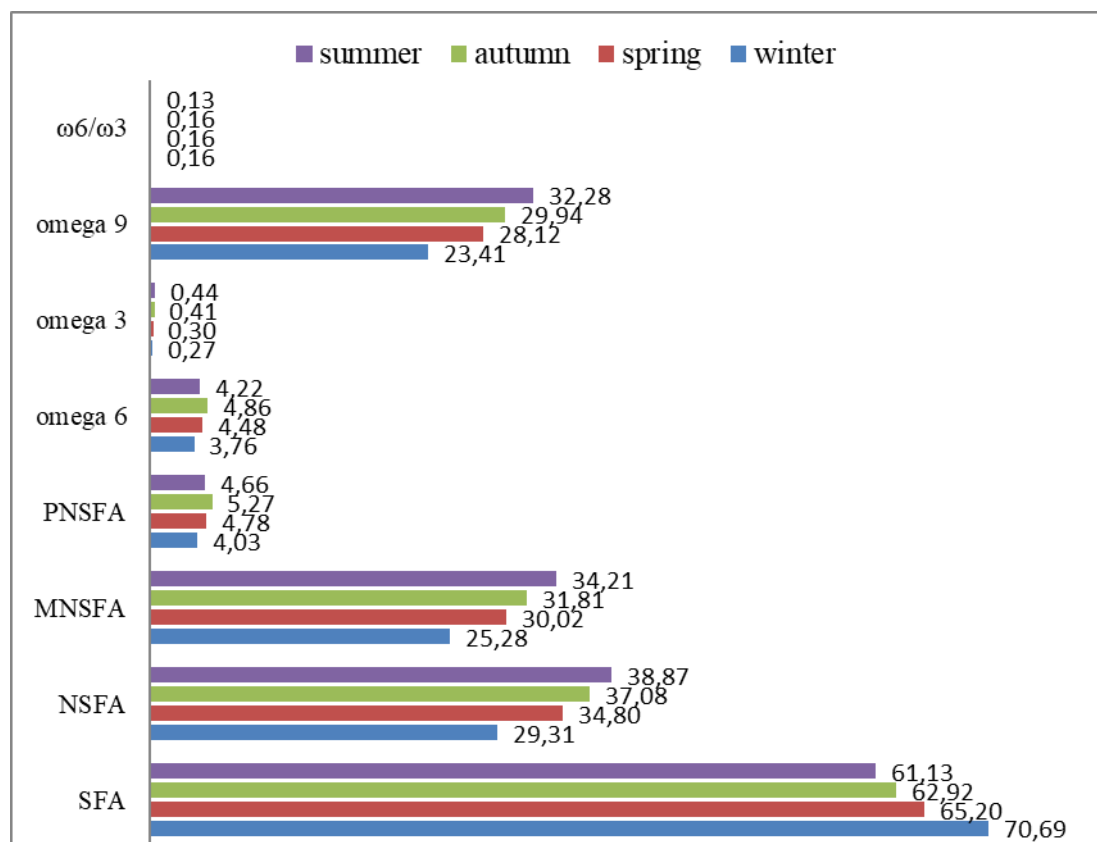


Fig. 1. The ratio of individual groups of fatty acids in raw milk depending on the season

As can be seen from Fig. 1. in summer the highest content of milk was NSFA, MNSFA and omega 9, in autumn the content of omega 6 was slightly higher, in spring all indicators had an average level, in winter - the content of SFA was the highest in milk.

Conclusions. Organoleptic, physicochemical, sanitary and hygienic indicators (except for bacteria of the *Escherichia coli* group in summer and autumn) meet the current requirements and change depending on the season. So the color of milk from May to September has a pronounced yellowish tinge. The mass fraction of fat and protein is lowest in summer and highest in winter, which probably depends on the presence of green mass in the diet of cows and concentrated and dry feed.

The fatty acid composition of milk corresponds to the fatty acid composition of milk fat. The amount of saturated fatty acids in winter increases by 9.56% compared to summer. The presence of green mass and corn silage in the diet of cows in milk increases the content of unsaturated fatty acids omega 3.

Prospects for further research and the practical significance of the results is that the results can be used as a basis for formulating a diet to obtain milk with optimal content and ratio of fatty acids, which can become competitive in the market of raw milk for milk and dairy products improved chemical composition, dietary, functional products, baby food.

References

- Magan, J. B., O'Callaghan, T. F., Kelly, A. L., & McCarthy, N. A. (2021). Compositional and functional properties of milk and dairy products derived from cows fed pasture or concentrate-based diets. *Comprehensive Reviews in Food Science and Food Safety*, 20(3), 2769-2800. doi:10.1111/1541-4337.12751.
- Yamaguchi, M., Naito, T., Nagao, Y., Kabuyama, Y., Hashimoto, K., Azuma, N., & Maeda, I. (2017). Effect of increased feeding of dietary-linolenic acid by grazing on formation of the cis9, trans11-18:2 isoform of conjugated linoleic acid in bovine milk. *Animal Science Journal*, 88(7), 1006-1011. doi:10.1111/asj.12727.
- Bainbridge, M. L., Egolf, E., Barlow, J. W., Alvez, J. P., Roman, J., & Kraft, J. (2017). Milk from cows grazing on cool-season pastures provides an enhanced profile of bioactive fatty acids compared to those grazed on a monoculture of pearl millet. *Food Chemistry*, 217, 750-755. doi:10.1016/j.foodchem.2016.08.134
- Pegolo, S., Stocco, G., Mele, M., Schiavon, S., Bittante, G., & Cecchinato, A. (2017). Factors affecting variations in the detailed fatty acid profile of Mediterranean buffalo milk determined by 2-dimensional gas chromatography. *Journal of Dairy Science*, 100(4), 2564-2576. doi:10.3168/jds.2016-11696.

- Barreiro, R., Regal, P., Diaz-Bao, M., Vazquez, B. I., & Cepeda, A. (2017). Effects of bovine pregnancy on the fatty acid composition of milk: the significance for humans needs. *Food Additives and Contaminants Part a-Chemistry Analysis Control Exposure & Risk Assessment*, 34(4), 608-616. doi:10.1080/19440049.2016.1277270
- Oliveira, M. X. S., Palma, A. S. V., Reis, B. R., Franco, C. S. R., Marconi, A. P. S., Shiozaki, F. A., Netto, A. S. (2021). Inclusion of soybean and linseed oils in the diet of lactating dairy cows makes the milk fatty acid profile nutritionally healthier for the human diet. *Plos One*, 16(2). doi:10.1371/journal.pone.0246357.
- Lanza, I., Lolli, V., Segato, S., Caligiani, A., Contiero, B., Lotto, A., & Cozzi, G. (2021). Use of GCeMS and 1H NMR low-level data fusion as an advanced and comprehensive metabolomic approach to discriminate milk from dairy chains based on different types of forage. *International Dairy Journal*, 123. doi: 10.1016/j.idairyj.2021.105174.
- Dias, K. M., da Gama, M. A. S., Schmitt, D., & Sbrissia, A. F. (2019). Milk fatty acid composition of unsupplemented dairy cows grazing on a tropical pasture. *Revista Brasileira De Zootecnia-Brazilian Journal of Animal Science*, 48. doi:10.1590/rbz4820190088.
- Silva, B., Rodriguez, N. M., Morenz, M. J. F., Gomide, C. A. D., Martins, C. E., Paciullo, D. S. C., & Lopes, F. C. F. (2018). Fatty acid composition of milk from Holstein x Gyr cows grazing on marandu grass supplemented with concentrate containing sunflower oil. *Semina-Ciencias Agrarias*, 39(6), 2581-2596. doi:10.5433/1679-0359.2018v39n6p2581.
- Musayeva, K., Sederevicius, A., Monkeviciene, I., Zymantiene, J., Oberauskas, V., Kerziene, S., Zelvyte, R. (2021). Milk fatty acid profile in cows as influenced by diet supplementation with rapeseed pomace and extruded full-fat soya in different feeding periods. *Acta Veterinaria Brno*, 90(1), 27-34. doi:10.2754/avb202190010027.
- Ministry of Agrarian Policy and Food. Vymohy do bezpechnosi ta yakosi moloka i molochnykh produkiv [Requirements for safety and quality of milk and dairy products]. № 118. (2019). Retrieved from <https://zakon.rada.gov.ua/laws/show/z0593-19#Text>
- Yakubchak, O. M., Taran, T. V., Ushkalov, V. O., Midyk, S. V., Berlous, K. O. (2021). Physicochemical and microbiological research of raw-milk material. *Ukrainian Journal of Veterinary Sciences* 12 (2), 26–37. <http://doi.org/10.31548/ujvs2021.02.003>
- Yakubchak, O. M., Laposha, O. A., Midyk, S. V., Taran, T. V., Zabarna I. V. (2018). Assessment of the Conformity of the Methods for Aflatoxin B₁ and Deoxynivalenol Determination in Grain and Feeds by Method of High-Performance Liquid Chromatography. *Methods and objects of chemical analysis*, 13 (3), 121–130. DOI: 10.17721/moca.2018.121-130
- Commission Regulation (EU) № 165/2010 of 26 February 2010 amending Regulation (EC) № 1881/2006 Setting maximum levels for certain contaminants in foodstuffs as regards aflatoxins <https://eur-lex.europa.eu/eli/reg/2010/165/oj/eng>
- Nakaz MON № 368 vid 13.05.2013. (2013). Derzhavni hiihienichni pravyla i normy "Rehlement maksimalnykh rivniv okremykh zabrudniuiuchykh rehovyn u kharchovykh produktakh". Dodatok. Hlava 2. Mikotoksyny. [Order of the Ministry of Education and Science № 368 dated 13.05.2013. State hygienic rules and norms "Regulations of maximum levels of certain contaminants in food". Addition. Chapter 2. Mycotoxins]. <https://zakon.rada.gov.ua/laws/show/z0774-13#n16>.
- Pu, J. H., Vinitchaikul, P., Gu, Z. B., Mao, H. M., & Zhang, F. L. (2021). The use of metabolomics to reveal differences in functional substances of milk whey of dairy buffaloes raised at different altitudes. *Food & Function*, 12(12), 5440-5450. doi:10.1039/d0fo03231j.
- Prosser, C. G. (2021). Compositional and functional characteristics of goat milk and relevance as a base for infant formula. *Journal of Food Science*, 86(2), 257-265. doi:10.1111/1750-3841.15574.
- DSTU ISO 707:2002 (ISO 707:1997, IDT) (2002). Moloko ta molochni produkty. Nastanovy z vidbyrannia prob. [Milk and dairy products. Instructions for selecting samples]. Kyiv: DP "UkrNDNTs".
- DSTU 8553:2015 Moloko-syrovyna ta vershky-syrovyna. Pravyla pryimannia, vidbyrannia ta hotuvannia prob do kontroliuvannia [Raw milk and raw cream. Rules for acceptance, sampling and preparation of samples for control]. Kyiv: DP "UkrNDNTs".
- Folch, J., Leez, M., Stanley, G. A. (1957). Simple Method for the Isolation and Purification of Total Lipides from Animal Tissues. *J. Biol. Chem.*, 226 (2), 497-501.
- DSTU ISO 5509–2002 (2002). Zhyry tvarynni i roslynni ta olii. Pryhotuvannia metylovykh efiriv zhyrnykh kyslot [Animal and vegetable fats and oils. Preparation of methyl esters of fatty acids] Kyiv: DP "UkrNDNTs".
- DSTU ISO 5508:2001. (2001). Zhyry ta olii tvarynni i roslynni. Analizuvannia metodom hazovoi khromatohrafii metylovykh efiriv zhyrnykh kyslot [Animal and vegetable fats and oils. Analysis by gas chromatography of fatty acid methyl esters] Kyiv: DP "UkrNDNTs".

DSTU 3662:2018. (2018). Moloko-syrovyna koroviache. Tekhnichni umovy [DSTU 3662:2018 Raw cow's milk. Specifications]. Kyiv: DP "UkrNDNTs".

Paredes, C.L.L., Werteker, M., Rossmann, B., Keplinger, J., Olschewski, I. L., Schreiner, M. (2018). Discrimination of haymilk and conventional milk via fatty acid profiles. Journal of Food Measurement and Characterization, 12, 1391–1398. <https://doi.org/10.1007/s11694-018-9753-0>.

ЯКІСТЬ МОЛОКА-СИРОВИНИ ТА ЙОГО ЖИРНОКИСЛОТНИЙ СКЛАД

О. М. Якубчак, Т. В. Таран, С. В. Мідик, В. В. Данчук, Н. Я. Дудченко, Л. М. Виговська

Анотація. Вивчення впливу пори року на органолептичні та фізико-хімічні показники молока і досі залишається актуальним. Крім того, співвідношення жирних кислот у молоці корів характеризує рівень їх годівлі та дослідження цих показників є актуальним з огляду на поширення фальсифікації молока і молочних продуктів рослинними оліями. Метою було дослідження окремих показників якості молока-сировини залежно від пори року та його жирнокислотного складу. **Матеріали і методи.** Матеріалом для дослідження слугувало збірне охолоджене молоко-сировина, отримане в різні пори року на молочно-товарній фермі ВП НУБіП України "Агрономічна дослідна станція". Дослідження проводили в акредитованій Українській лабораторії якості і безпеки АПК НУБіП України. Органолептичні, фізико-хімічні, санітарно-гігієнічні визначали загальноприйнятими стандартними методами. Жирнокислотний склад молока досліджували методом газової хроматографії. Екстракцію ліпідів з молока проводили за методом Фолча. Аналіз метилових ефірів ЖК проводили на газовому хроматографі Trace GC Ultra (США) з полум'яно-іонізаційним детектором. Ідентифікування жирних кислот проводили за допомогою стандартного зразка Supelco 37 Cotropept FAME Mix. Кількісну оцінку спектру жирних кислот ліпідів молочного жиру здійснювали методом внутрішньої нормалізації з визначенням їх у відсотках. Дослідження проводили у 2-х паралелях. Статистичну обробку експериментальних даних проводили загальноприйнятими методами варіаційної статистики. Вірогідність різниці показників оцінювали за *t*-критерієм Ст'юдента. Відмінності між показниками, що порівнювались, вважали вірогідними за рівня значимості $P < 0,05$. **Результати і обговорення.** Проведені дослідження засвідчили, що молоко органолептичні та фізико-хімічні показники молока-сировини змінюються залежно від пори року. Щодо мікробіологічних показників, то молоко відповідало першому гатунку, хоча зимою за іншими показниками його можна було віднести до екстра, чи в гіршому випадку, до вищого гатунку. Крім того, взимку вміст насичених жирних кислот у молоці зростає. Влітку та восени підвищується вміст ненасичених жирних кислот, що пов'язано з наявністю у раціоні корів зеленої маси та кукурудзяного силосу. Отримані результати можна використовувати як основу для складання раціону з метою отримання молока з оптимальним вмістом і співвідношенням жирних кислот, що може стати конкурентним на ринку молока-сировини з метою виробництва молока і молочних продуктів поліпшеного хімічного складу, дієтичних, функціональних продуктів, дитячого харчування.

Ключові слова: молоко-сировина, якість, санітарно-гігієнічні показники, жирні кислоти

PATHOMORPHOLOGICAL CHANGES IN CATS WITH CHLAMIDIOSIS

N. B. KOLYCH, Candidate of Veterinary Sciences, Associate Professor
Academician V. G. Kasyanenko Department of Anatomy, Histology and Pathomorphology
<https://orcid.org/0000-0001-8024-0810>

N. HUDZ, Candidate of Veterinary Sciences, Senior Researcher

Institute of Veterinary Medicine NAAS

<https://orcid.org/0000-0001-8024-0810>

National University of Life and Environmental Sciences of Ukraine, Kyiv, Ukraine

E-mail: Natasha-vet@ukr.net

Abstract. *In recent years, there is a tendency to increase the incidence of the disease in dogs with signs of diarrhea, not only in Ukraine, but also in Europe. In general, diseases with the manifestation of such specific clinical sign as diarrhea can be caused by viruses, bacteria and helminths. In general pathology of dogs, enterovirus infections of puppies occupy a leading place. The practice of specific prophylaxis suggests that in the etiological aspect diseases emerging with this symptom can be caused not only by parvo-, but also corona- and rotavirus enteritis. These diseases are extremely dangerous for puppies and miniature dogs, due to rapid dehydration, and as a result, death.*

The article presents the results of a study on histological changes in organs and tissues of dogs with coronavirus infection. A histological study of pathological material sampled from 6 dogs of various breeds and sex, aged from 2 to 6 months, died from diarrheal syndrome was carried out. The presence of the coronavirus was confirmed in fecal samples by polymerase chain reaction.

The most expressed injuries and typical changes in all dead dogs we recorded in the small intestine, namely in the jejunum and ileum, regional lymph nodes, and also in the spleen.

Morphological manifestations of coronavirus infection in dogs at macroscopic level are the following signs: the presence of exudative inflammation in the small intestine in form of serous-fibrinous jejunoileitis, hyperplasia and serohemorrhagic lymphadenitis of the mesenteric lymph nodes, multiple foci of hemorrhage in the parenchyma of the spleen and serous membrane of the small intestine, passive venous hyperemia of the liver and kidneys, dilatation of the right ventricle of the heart, pulmonary edema, cachexia and dehydration of the body.

At the microscopic level we registered the following: serofibrinous jejunoileitis, hyperplasia of the lymphoid nodules of the spleen and lymph nodes, hemorrhagic infarctions in the spleen, hyperplasia of individual and aggregated lymphoid nodules of the mucous membrane in the small intestine, degenerative processes in the parenchyma of the liver and kidneys.

Key words: *coronavirus infection, dogs, histological changes, hemorrhages, serofibrinous jejunoileitis, serohemorrhagic lymphadenitis, hyperplasia, lymphoid nodules.*

Introduction

The main threat to global health, economic stability and national security is zoonotic viral diseases, both known and re-emerging (R. L. Graham, D. J. Deming, M. E., 2018). The emergence of zoonoses can be considered a logical consequence of the ecology and evolution of pathogens that use new niches and adapt to new hosts.

Due to the constant human interference with the animal habitat and our close contact with domestic animals, the number of zoonoses will continue to increase, given the spread and density of population and livestock production over the next century.

In developed countries, the problem of infectious pathology of small domestic animals, as well as in ours, has its own stages of exacerbation, since pathogens evolve, adapt, occupy new niches and, thus, do not allow to weaken our attention to them. At the same time, there is a lack of domestic literature devoted to the problems of infectious pathology of small animals, presented with consideration of modern data obtained by scientists on a global scale.

More than 60% of infectious diseases in humans are caused by pathogens inherent in wild or domestic animals. Microorganisms that cause zoonoses include those that are endemic in human populations or enzootic in animal populations with frequent interspecies transmission to humans (W. B. Karesh, A. Dobson, 2012). The role of viruses in the emergence and development of human infectious diseases is growing steadily. Only at the beginning of the 21st century, many new viruses appeared,

which were not previously known, and most of which are able to cause severe infectious diseases, often fatal.

Among them are new human coronaviruses, which are called SARS-CoV (Severe acute respiratory syndrome, SARS) and MERS-CoV (Middle East respiratory syndrome, MERS). Both of them cause acute respiratory distress syndrome (ARDS) and are associated with high mortality rates (S. Su, G. Wong at all, 2016).

In N. Decaro and C. Buonavoglia (2008) review on the genetic evolution of CCoV and the emergence of new CoVs in canines, it is also noted that the emergence of severe acute respiratory syndrome in humans has provoked new interest, to animal coronaviruses as well, as potential agents of direct and indirect zoonoses .

Analysis of recent research and publications

Canine coronavirus (CCoV), has been known since the 1970s. In dogs, CoV is associated with mild enteritis. But CoV strains with different biological and genetic properties in relation to the classic CCoV strains have been found in dogs in recent years, leading to a complete reconsideration of the CoV-induced canine diseases.

The practice of specific prophylaxis allows us to state that in the etiological aspect, diseases emerging with this symptom can be caused not only by parvo-, but also corona- and rotavirus enteritis. S.A. Godsall et al. (2010) also noted that canine parvovirus (CPV) and canine enteric coronavirus (CECoV) are usually cause diarrhea in dogs. Although the canine enteric coronavirus is less common, it still remains a potentially important pathogen, the authors noted (Godsall S.A,2010). These diseases are extremely dangerous for puppies and miniature dogs, due to rapid dehydration and, as a consequence, death.

The name “coronavirus” dates back to 1968 and derives from the Greek κορώνα, which means corona (corona-like structure observed in these viruses in an electron microscope). Coronaviruses (CoVs) are enveloped viruses with spherical, and sometimes pleomorphic virions with a diameter of 80 to 120 nm. Coronaviruses have the largest genomes of all RNA-viruses known today with an average length of 27 to 31 thousand bp and replicate using a unique mechanism, which leads to a high frequency of recombinations (X. Wang, C. Li, D. Guo et al.2016).

Previously, coronaviruses were divided into three genera (I-III), which were usually called groups and based on serological cross-reactivity (Pratelli A. , 2011).

Phylogroup I CoV including human coronaviruses HCoV-229E and HCoVNL63 that cause respiratory infections, feline coronaviruses (FCoVs) type 1 and 2, transmissible gastroenteritis virus (TGEV) of pigs, porcine respiratory coronavirus (PRCoV), porcine epidemic diarrhea virus (PEDV), and canine coronaviruses (CCoVs). Ferret coronavirus has recently been identified as a member of phylogroup I.

Phylogroup II of the mammalian CoV is divided into two subgroups, bovine-like subgroup 2a and SARS-like subgroup 2b. Subgroup 2a includes bovine coronavirus (BCoV), murine hepatitis virus (MHV), sialodacryoadenitis virus of rats (SDAV), porcine hemagglutinous encephalomyelitis virus (PHEV), human coronaviruses (HCoV-OC43 and HCoV-HKU1), which cause respiratory infections, human enteric coronavirus (HECV-4408), the recently recognized equine coronavirus (ECoV) and canine respiratory coronavirus (CRCoV).

Group III includes only avian coronaviruses, such as infectious bronchitis virus (IBV), turkey coronavirus (TCoV) and pheasant coronavirus.

Canine coronavirus (CCoV) causes sporadic cases of enteritis in dogs. In general, CCoV is recognized as the etiological agent of self-limiting small intestine infections, which can lead to mild gastroenteritis. Mild illness or asymptomatic carrier state are likely to be the usual consequences of infection in most cases. Canine coronavirus enteritis (CCoV) is a common infection, usually in young dogs, especially those in large groups such as dog pounds, shelters and kennels (Stavisky, G. Pinchbeck, RM. Gaskell et al., 2012). However, several years ago, a highly virulent strain (pantropic CCoV) was isolated that caused an outbreak of fatal, systemic diseases in puppies. This strain showed some genetic changes relative to the existing strains circulating in the dog population. By definition, 53 feline and canine coronaviruses are common pathogens in cats and dogs that can cause fatal infections such as feline infectious peritonitis (FIP) and canine pantropic coronavirus infection. Alphacoronavirus coronavirus and Betacoronavirus respiratory coronavirus have been found in dogs (T. Takano, S. Yamashita, M. Murata-Ohkubo at all. 2016).

The extent of the natural disease caused by canine coronavirus is not well understood, as the pathogenesis of CCoV is not yet well defined. It was previously reported that the infection was associated with moderate to severe gastroenteritis, but it now appears that CCoVs are predominantly mild or subclinical, with low mortality rates.

CCoV is acid resistant, so it passes through the stomach unchanged. Viremia and generalized infection are not observed. The superficial epithelium of the small intestine is the main target of CCoV, but the large intestine is resistant to infection. In 2 days after oral infection, CCoV can be detected in the cytoplasm of mature epithelial cells of the villi in the upper two-thirds of the duodenum, compared to canine parvovirus type 2 (CPV-2), which destroys the epithelium of intestinal crypts.

Loss of villi of mature enterocytes causes atrophy of intestinal villi and, as a consequence, weakening of the integrity of the intestinal barrier [54]. After the fourth day of infection, the small intestine usually has a heterogeneous distribution of infected villi [68]. Together these changes in the morphology of the small intestine result in a loss of normal digestive and absorption functions, as well as clinical signs of diarrhea and dehydration in sick dogs.

The factors regulating the course of natural diseases caused by intestinal CCoVs are not well understood. CCoVs are responsible for enteritis in dogs, and signs of infection can range from mild to moderate, but more severe in young puppies or in combination with other pathogens. All data raise a number of questions and request deeper studies of the pathobiology of CCoVs types 1 and 2.

Material and methods of research.

The study was performed in the pathohistological laboratory of the the Academician V.G. Kasyanenko Department of Anatomy, Histology and Pathomorphology of Animals of the Faculty of Veterinary Medicine of NULES of Ukraine.

The material of the study was the pathological material collected during the postmortem autopsy of dogs of various breeds and genders who died with diarrheal syndrome at the age from 2 to 7 months (n = 6). The presence of coronavirus, with no other pathogens, was confirmed in fecal samples of dogs before death by PCR. According to the anamnestic data, animals had pronounced clinical signs such as the disruption of the digestive system of an infectious origin (fever, lack of appetite, vomiting, diarrhea). The pathological and anatomical autopsy of the dogs' carcasses was performed in the supine position by the method of partial evisceration in the generally accepted sequence.

The main method used in the study was histological examination, during which microstructural changes in organs and tissues were recorded and described. The pathological material was processed according to generally accepted histological methods.

Pieces of organs were fixed with a 10% Neutral Buffered Formalin according to Lilly's prescription, graded alcohols were used for dehydration and embedded in paraffin after chloroform. Using a sled microtome, sections with a thickness of 6-7 μm were obtained. The histological structure of organs and tissues was studied by sections' staining with Karazzi's hematoxylin and eosin. The histopreparation was examined and photographed using an Olympus microscope BX-41 (L.P. Goralskij, M L. Radzihovskij, S. S. Zayika 2018).

Research results and discussion.

On external examination of the dead animals' carcasses in all cases we noted dull coat, the skin was dry, not elastic, the visible mucous membranes were dry, pale with a grayish color, not shiny. All animals showed signs of malnutrition as a result of dehydration and diarrhea.

The liver was enlarged, elastic, dark cherry color with insignificant areas of putrefactive color, which indicated the presence of dystrophic processes in its parenchyma. A red, bloody fluid flowed from the incision. Histological examination revealed the destruction of the beam structure of the liver. Hepatocytes are placed randomly with signs of granular dystrophy, which was morphologically manifested by cells' swelling, disappearance of cytoplasm transparency, and appearance of protein origin grains. Hepatocytes showed signs of karyolysis. Sinusoidal capillaries were engorged with blood in the center of the lobules. In the lumen of the central veins there were formed elements of blood, mainly erythrocytes. In some cases, small areas of fatty degeneration were found with the formation of characteristic vacuoles of various sizes in the cells' cytoplasm.

The gallbladder in all cases was filled with thick dark green bile.

The pancreas was of gray-pink color, slightly enlarged, edematous. The lobulated structure was well-defined.

The spleen was moderately enlarged, had soft texture with pointed edges. Hemorrhagic infarcts were registered on the surface of the spleen.

Microscopically, the red pulp showed hemorrhages and clear contours and a specific triangular structure of hemorrhagic infarcts. On the section, a pronounced granular structure of the organ was shown by hyperplastic lymphoid nodules due to active proliferation of lymphoid cells.

The kidneys in all cases were dark cherry in color. On the section, the border between the cortical and medullary substances was smoothed, the section surface had increased moisture. It should be noted that venous hyperemia of the liver and kidneys was the result of hemodynamic disturbances in the systemic circulation due to heart failure. The main microscopic changes of a dystrophic nature were found in the epithelium of the convoluted tubules. The affected epithelium is massively desquamated into the lumen of the tubules.

The heart is enlarged in size, round in shape due to the right ventricle enlargement, less often the entire right side, and due to the displacement of the heart apex to the left. The heart muscle was soft, unevenly colored, a gray-pink color. The cut surface had increased moisture, the blood vessels of the heart were full of blood. Such pathological processes may indicate the development of compensated heart failure during the life of the animal, which developed as a result of the disease.

Lungs had even red color, pastry, elastic consistency, the pieces floated difficult in water. A foamy reddish liquid flows down from the cut surface. The same fluid was in the trachea and in the lumen of large bronchi that was a morphological sign of pulmonary edema due to venous hyperemia.

Examination of the abdominal organs in all cases showed enlarged mesenteric lymph nodes, vascular hyperemia and hemorrhages in the serous membrane of the intestine. On the cut, the parenchyma of the lymph nodes was pink-red, juicy, and shiny. Signs of serohemorrhagic inflammation were noted in the form of serous impregnation of the lymph node parenchyma and the release of formed blood cells with exudate.

Microscopically the lymphoid nodules hyperplasia of lymph nodes was shown as a result of active proliferation of reticulocytes and lymphoid cells. In some nodules necrosis and devastation were observed.

Along the entire length of the small intestine, striped, less often spotted hemorrhages appeared on the serous membrane. The content of the small intestine, in particular the jejunum and ileum, looked like a cloudy gray-pink fluid. The surface of the mucous membrane of the jejunum and ileum was covered with a large amount of liquid cloudy mucus, under which small spotty hemorrhages were manifested. In the cut, the wall of the small intestine was edematous and gelatinous. In some cases, pityriasis with gray-yellow films were noted on the mucous membrane of the jejunum and ileum that were difficult to remove (Fig.1).



Figure 1. Catarrhal-hemorrhagic inflammation of the small intestine

In the jejunum, an increase in the lymphoid formations of the intestinal wall was observed: rare and aggregated lymphoid nodules due to the proliferation of reticulocytes and the accumulation of a large number of lymphocytes. They acquired a clear rounded shape and were intensively stained with hematoxylin. The main changes were localized mainly in the villi area. Effusion of fibrinous exudate was observed on the surface of the mucous membrane, which, together with the desquamated epithelial cells, covered the villi in the form of lumps. In epithelial cells there were karyopyknosis, karyorrhexis and signs of cytolysis. Necrosis and loss of the epithelium of the villi of the small intestine were accompanied with their atrophy, deformation, shortening and desquamation of the virus-infected enterocytes into the lumen (Fig. 2).

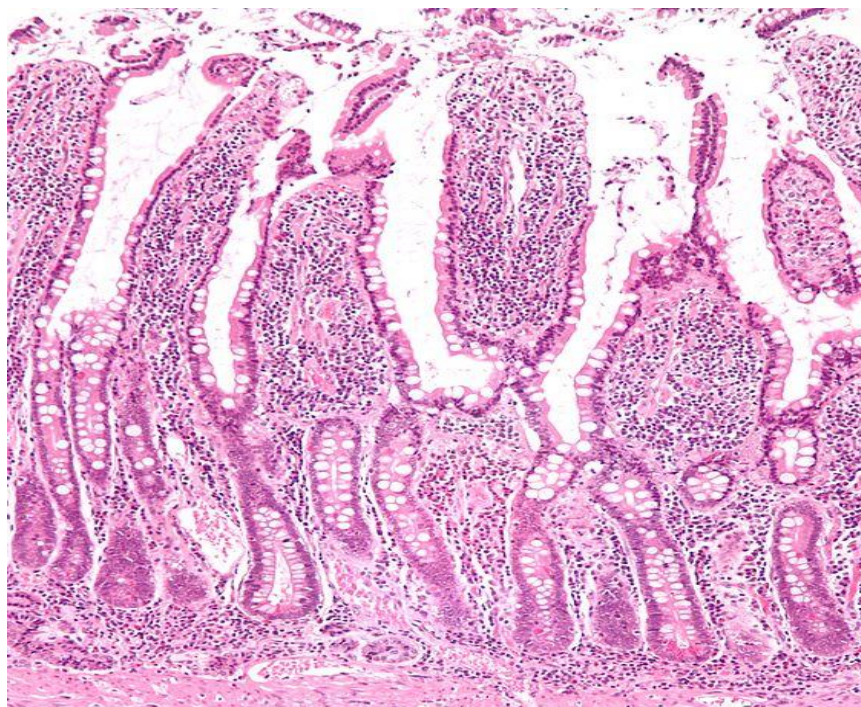


Figure 2. Desquamation of the epithelium, deformation and destruction of villi. Hematoxylin and eosin. 400x.

Along with expressive alterative changes in the epithelium, regeneration processes were often clearly expressed, mainly in crypt areas. There were no significant histological changes. The structure of the crypts and the epithelium was preserved. Necrosis and loss of epithelium of the villi of the small intestine and the probable disruption of goblet cell secretion leads to the destruction of its protective barrier. Diarrheal syndrome is one of the main clinical manifestations and a key link in the pathogenesis of coronavirus infection is due to the development of serofibrinous enteritis, since in the areas of inflammation there is a loss of mature epithelium, parietal digestion and cellular absorption are disturbed.

Conclusions

1. Morphological manifestations of coronavirus infection in dogs at the macroscopic level are: serofibrinous jejunoileitis, hyperplasia and serohemorrhagic lymphadenitis of mesenteric lymph nodes, dilatation of the right ventricle of the heart, multiple hemorrhages in the spleen parenchyma and in the serous membrane of the small intestine, cachexia and dehydration of the body.

2. At the microscopic level, the following was noted: serofibrinous jejunoileitis, hyperplasia of the lymphoid nodules of the spleen and lymph nodes, hemorrhagic infarcts in the spleen, hyperplasia of individual and aggregated lymphoid nodules of the mucous membrane of the small intestine, passive venous hyperemia of the liver and kidneys, dystrophic processes in the parenchyma of the liver and kidneys.

Prospects for further research. For a complete study of the pathomorphological picture of coronavirus enteritis in dogs, as the next stage, it is advisable to investigate the characteristics of this disease using histochemical methods.

References

Ann S.Y., Kim H.T., Kim, D. (2014). M gene analysis of canine coronavirus strains detected in Korea. J Vet Sci. 15, 495–502.

- Decaro, N., Mari, V., von Reitzenstein, M. (2012). A pantropic canine coronavirus genetically related to the prototype isolate CB/05. *Vet Microbiol.* 159 (1–2), 239–244.
- Gizzi, A.B.R., Oliveira, S.T., Leutenegger, C.M. et al. (2014). Presence of infectious agents and co-infections in diarrheic dogs determined with a real-time polymerase chain reaction-based panel. *BMC Veterinary research*, 6, 81–90.
- Goralskij, L.P., Homych, V.T., Kononskij, O.I. (2011). *Osnovy histologichnoyi tehniky i morfofunkcionalni metody doslidjen u normi ta pry patologiyi* [Foundations of histological engineering and morphofunctional methods of research in norm and pathology]. Jytomir, Ukrainian: Polissya (in Ukrainian).
- Godsall S.A. Epidemiology of canine parvovirus and coronavirus in dogs presented with severe diarrhoea to PDSA / Godsall SA, Clegg SR, Stavisky JH // *Pet Aid hospitals. Vet Rec.* – 2010. – 167. – P. 196–201, doi: 10.1136/vr.c3095.
- Graham R. L. Evaluation of a recombination-resistant coronavirus as a broadly applicable, rapidly implementable vaccine platform / R. L. Graham, D. J. Deming, M. E. Deming, B. L. Yount, R. S. Baric // *Communications Biology.* – 2018. – V. 1. – Article number: 179. Режим доступу: <https://www.nature.com/articles/s42003-018-0175-7>
- Karesh W. B. Ecology of zoonoses: natural and unnatural histories / W. B. Karesh, A. Dobson, J. O. Lloyd-Smith et al. // *Lancet*, 2012. – V. 380. – P. 1936–1945.
- Pratelli A. The Evolutionary Processes of Canine Coronaviruses / A. Pratelli // *Advances in Virology.* – Vol. 2011. – Article ID 562831, 10pages.doi.org/10.1155/2011/562831. Режим доступу: <https://www.hindawi.com/journals/av/2011/562831/>
- Stavisky J. Cross sectional and longitudinal surveys of canine enteric coronavirus infection in kennelled dogs: a molecular marker for biosecurity / J. 125 Stavisky, G. Pinchbeck, RM. Gaskell et al. // *Infect Genet Evol.* – 2012. – 12. – P. 1419–1426.
- Su S. Epidemiology, Genetic Recombination, and Pathogenesis of Coronaviruses / S. Su, G. Wong, W. Shi, J. Liu, A. C.K. Lai et all. // *Trends in microbiology.* – 2016. – 24 (6). – P. 490-502.
- Takano T. Prevalence of canine coronavirus (CCoV) in dog in Japan: detection of CCoV RNA and retrospective serological analysis / T. Takano, S. Yamashita, M. Murata-Ohkubo, K. Satoh, T. Doki and T. Hohdatsu // *J Vet Med Sci.* – 2016. – 78(2). – P. 341–345.
- Wang, X., Li, C., Guo, D. (2016). Co-Circulation of Canine Coronavirus I and IIa/b with High Prevalence and Genetic Diversity in Heilongjiang Province, Northeast China. Available at: <http://journals.plos.org/plosone/articleid=10.1371/journal.pone.0146975> Jeoung,

CLINICAL EFFICACY OF PHOSPHOLIPID-CONTAINING PREPARATIONS OF DIFFERENT ORIGIN UNDER EXPERIMENTAL GASTROENTEROPATHOLOGY IN MICE

V. A. Gryshchenko, Doctor of Veterinary Sciences, Professor,
Department of Animal Biochemistry and Physiology named after Academician M. F. Gulyi
<https://orcid.org/0000-0001-6601-1392>
National University of Life and Environmental Sciences of Ukraine, Kyiv, Ukraine
E-mail: viktoriya_004@ukr.net

J. Illek, Associate Professor MVDr., DrSc., Dipl. ECBHM, Professor,
Faculty of Veterinary Medicine, Large Animal Clinical Laboratory
<https://orcid.org/0000-0002-1374-7918>
University of Veterinary Sciences Brno, Brno, Czech Republic
E-mail: illekj@vfu.cz

V. A. Tomchuk, Doctor of Veterinary Sciences, Professor,
Department of Animal Biochemistry and Physiology named after Academician M. F. Gulyi
<https://orcid.org/0000-0003-0622-6345>
National University of Life and Environmental Sciences of Ukraine, Kyiv, Ukraine
E-mail: tomchuk_viktor@ukr.net

Abstract. Diseases of the digestive system are extremely common among animals, especially young animals. The purpose of this work was to determine the features of the corrective effectiveness of reparative agents based on phospholipids of various origins based on the results of a comprehensive study of clinical, hematological, immunological parameters and the structural and functional state of immunocompetent organs in CBA mice with experimental gastroenteropathology.

As a result of the reproduction of an acute form of hemorrhagic gastroenteritis with diarrheal syndrome in CBA mice, the development of characteristic clinical symptoms was noted. Regardless of the nature of the origin of phospholipids, preparations based on them exhibited a pronounced reparative effect on cell damage. At the same time, the effectiveness of the dietary supplement "FLP-MD" based on phospholipids from milk according to some indicators turned out to be better than the preparation Essentiale-forte based on phospholipids from soybeans. Thus, the peculiarity of the effect of the dietary supplement "FLP-MD" on the organism of sick mice is the acceleration of the restoration of the general clinical state of the animals (on the 8-10th day from the beginning of the introduction of the dietary supplement into the body versus the 10-12th day when using the drug essentiale-forte), restoration of the mass of lymphoid organs (thymus and spleen); an increase in the relative number of T-lymphocytes in the blood by 1.4 times due to the activation of proliferative processes in the organs of the immune system (4.8 times in the spleen, 1.5 times in the thymus).

Keywords: experimental gastroenteropathology, laboratory mice of the CBA line, clinical, hematological, immunological, microscopic studies, phospholipids from milk and soy, correcting efficiency

Introduction

Animal gastroenteropathology remains the most common group of diseases of the digestive system, prompting the development of effective drugs and the introduction of new therapeutic regimens. Animals of all species and age groups are affected, but more often young animals (Sato, 2010). More and more attention is paid to the intensive correction of structural and functional disorders of organs and tissues damaged during the development of gastroenteropathology (Szabo et al., 2007; by Abdel Khalek et al., 2012; Tomchuk, V. et al., 2019).

In clinical medicine, the leading role in the development of a severe course of diseases of the digestive, nervous and cardiovascular systems, disorders of the structural organization of the lipid bilayer of membranes and the effectiveness of the use of reparative drugs for its restoration has already been proven (Bothra et al., 2018; Leskova et al., 2020). Among such agents, phospholipid-containing drugs occupy a leading place (Harvey & Cave, 2014; Yang et al., 2018; Gryshchenko, 2020). The membrane stabilizing and protective action of phospholipids is achieved by their direct incorporation into the phospholipid structure of damaged cell membranes, replacing defects and restoring the barrier function of their lipid bilayer.

Exogenous phospholipids promote the activation of phospholipid enzymes located in the membrane, and significantly support intracellular metabolism. The protective action of these compounds is also based on the inhibition of lipid peroxidation, which is considered one of the leading pathogenetic mechanisms of organ and tissue damage (Solís-Calero et al., 2015; Colombo et al., 2018; Gryshchenko et al., 2018).

Phospholipids, which are part of modern medicines, mainly of plant origin and obtained from soy. However, they differ in their chemical structure from the phospholipids of the cell membranes of the human and animal body. Therefore, the idea arose to create a bioadditive of reparative action ("FLP-MD") based on phospholipids of animal origin, namely from milk, which in their chemical structure correspond to such lipid components of mammalian cell membranes.

Analysis of recent research and publications

High clinical efficacy, almost complete absence of contraindications to the use and non-toxicity of phospholipid drugs contributed to their intensive use in the practice of phthisiatric, pulmonary surgical, cardiological and intensive care units, as well as in gastroenterology for the correction of functional disorders of the liver and organs of the gastrointestinal tract in humans (Bothra et al., 2018; Colombo et al., 2018; Zhang et al., 2018). Thus, in gastroenteritis, regardless of the etiology of the onset of the disease, there is a violation of the structural organization of the epithelial layer of the mucous membranes of the digestive tract, primarily, this concerns the plasmolema of epithelial cells (Deng et al., 2009; Qingbiao et al., 2014). Therefore, in clinical practice, it is advisable to use drugs that stimulate reparative processes, and their active substances easily penetrate the cell membranes of the digestive organs and show tropism to cell membranes (primarily, drugs based on phospholipids and essential fatty acids). There are practically no therapeutic and prophylactic agents with a reparative effect on the market of veterinary drugs. Thus, the use of reparative phospholipid-containing drugs in veterinary medicine requires detailed study and is relevant.

The aim of this work is to determine the features of the corrective effectiveness of reparative agents based on phospholipids of various origins based on the results of a comprehensive study of clinical, hematological parameters and the structural and functional state of immunocompetent organs in CBA mice with experimental gastroenteropathology.

Materials and methods of research

The studies were carried out on sexually mature mice of both sexes of the CBA line breeding the vivarium of the Ukrainian Research Institute of Oncology and Radiology of the Ministry of Health of Ukraine, laboratory studies were carried out on the basis of the laboratory of the Research Department of Clinical Immunology of this institute. For the experimental reproduction of the acute form of gastroenteropathology in mice, the following model was used: during the first five days, the drug Guttalax was administered per os once a day at a dose of 0.75 mg/kg of body weight, and then, for two days, an aqueous solution of diclofenac was administered per os dose of 25 mg/kg body weight (Melnychuk, 2008). This model corresponds to the development of hemorrhagic gastroenteritis with diarrheal syndrome. After the reproduction of gastroenteropathology in laboratory animals, from the eighth day of the experiment, corrective therapy was started in the form of a liposomal form of a phospholipid-containing biologically active additive (BAA) "FLP-MD" (Melnychuk et al., 2009) - 2 g/kg of body weight per day and the drug essentielle-forte for injection – 67 mg/kg of body weight per day, which was administered per os for 30 days.

Experimental groups consisted of ten mice (five of each sex): up to group I included intact animals, to group II - animals in a state of experimentally recreated gastroenteropathology, without treatment (control), in group III - animals in a state of experimental gastroenteropathology using as corrective therapy of essentielle-forte based on soy phospholipids, in group IV mice were in a state of experimental gastroenteropathology, which underwent correction of dietary supplements "FLP-MD" based on milk phospholipids. The main phospholipids of the membranes of milk fat globules are phosphatidylcholine, phosphatidylethanolamine and sphingomyelin, which account for more than 80% of the total lipid phosphorus. Phosphatidylserine, phosphatidylinositol and lysophospholipids are contained in globules in small and unstable amounts. The fatty acid composition of neutral and polar lipids of the membranes of fatty globules of milk is mainly represented by palmitic, stearic, oleic and linoleic acids, which make up 84-90% of all fatty acids.

Changes in the general condition of the animals, dynamics of body weight, appetite, behavior, the amount of food consumed and mortality were monitored. After the end of the experiment (on the 37th day from the beginning), the mice were decapitated under ether anesthesia. Blood samples were taken from these

animals for hematological and immunological studies, the weights of the thymus and spleen, thymus and spleen indices (the ratio of organ weight (mg) to animal body weight (g), the number of lymphoid cells in the indicated immunogenesis organs) were determined. Microscopic examination Pieces of tissue were fixed in 10% formalin solution, and their sections were stained with hematoxylin-eosin.

The morphological study of the peripheral blood of the experimental animals included the preparation of smears, which were stained according to Romanovsky-Giemsa, to display the leukogram.

Thymic endocrine function was assessed by serum thymic factor (TSF) levels (Bach & Dardenne, 1973). The content of T-lymphocytes in the peripheral blood of mice was determined by the method of spontaneous rosette formation (E-ROK), which is based on the determination of the presence of receptors on the surface of T-cells for rabbit erythrocytes (Nicoletti et al., 1991).

A suspension of thymus and spleen cells was used to study spontaneous apoptosis and proliferation. We used a T-cell mitogen – phytohemagglutinin (PHA), which was used to activate splenocytes and thymocytes. The DNA content in cells was assessed by the protocyotometric method (FACScan "Becton Dickinson" USA device) after staining with a fluorochrome (propidium iodide), selectively binds to DNA in the cell nucleus (Moorhead, 1970). The index of proliferative activity (IPA) was determined by dividing the percentage of cells in the proliferative pool by the percentage of cells in a state of apoptosis.

The experimental data were statistically processed using the STATISTICA 5.0 software package (Stat Soft, USA) using Student's criteria with normal distribution. Differences between the data were considered significant at $P < 0.05$.

Results of the research and their discussion

From the first days of the reproduction of the acute form of gastroenteropathology in mice of the CBA line of research groups, the development of clinical symptoms of gastroenteropathology is noted: decreased mobility, depression of the general condition, exhaustion and loss of appetite, rarefied (creamy) consistency of feces. The severe form of this pathology is characterized by a high percentage of mortality in mice (84%), which decreases to 50% when using *essentiale-forte*, and when using dietary supplements "FLP-MD" - up to 8%.

The disappearance of the described clinical symptoms in experimental animals subject to self-rehabilitation (group II, control) is noted only on the 30th day of observation.

At the same time, in mice of the III group, the recovery of the level of food consumption was noted on the 2nd day of the rehabilitation period. An improvement in the clinical state of the animals was recorded on the 4-5th day from the start of the drug *essentiale-forte*, and on the 10-12th day, the behavior of these animals did not differ from that of intact mice. The increase in body weight in males was established on the 13th day, and in females much later, on the 30th day of administration of this drug.

In animals of group IV, a significant improvement in the functional state of the body - an increase in mobility and restoration of appetite was noted on the 3rd day from the beginning of the use of dietary supplements "FLP-MD". Already on the 8–10th day of the experiment, the behavior of these animals did not differ from the mice of group I. An increase in body weight was established in mice: in males after the seventh day from the beginning of the introduction of correction therapy, and in females on the 30th day of the experiment. The body weight in animals of the control group remained unchanged throughout the observation period.

The results of the study of hematological parameters in experimental CBA mice are presented in Table. 1.

As can be seen from the data obtained, in animals of group II in the peripheral blood, the number of erythrocytes and the content of hemoglobin does not differ from the level of intact animals, but the ESR significantly decreases. In animals of this group, there is also a decrease in the number of leukocytes by 35%, primarily in the relative and absolute number of monocytes (3.5 times) and segmented neutrophils (2.4 times).

After the application of corrective therapy in the form of *essentiale-forte* and the "FLP-MD" dietary supplement, a significant decrease in the level of hemoglobin in the blood was found in comparison with that in animals of groups I and II. This is probably due to the discrepancy between the intensity of the processes of erythrocytopoiesis and hemoglobin formation. The value of ESR in the group of animals receiving dietary supplements "FLP-MD", significantly increased, which may be due to an intensive increase in the mass of erythrocytes in the blood. The use of both *essentiale-forte* and the "FLP-MD" dietary supplement in experimental mice was accompanied by a significant decrease in the absolute number of monocytes (by 58%) in the peripheral blood of group III animals and in the relative blood by 2.6 times in

group IV mice.

1. Hematological parameters and the number of T-lymphocytes in the peripheral blood of experimental CBA mice (M ± SD, n = 6-8)

Index		Group of mice			
		I	II	III	IV
Erythrocytes, ×10 ¹² /L		6.16 ± 0.91	6.77 ± 0.88	7.72 ± 0.49	7.50 ± 0.23
Hemoglobin, g/L		128.00 ± 6.58	130.0 ± 2.00	115.00 ± 2.91**	110.33 ± 3.93***
Hematocrit, L/L		0.52 ± 0.03	0.49 ± 0.01	0.46 ± 0.02	0.48 ± 0.02
ESR, mm/hour		1.13 ± 0.13	0.05 ± 0.01*	1.00 ± 0.01**	1.38 ± 0.24**
Leukocytes, ×10 ⁹ /L		4.32 ± 0.35	2.80 ± 0.25*	2.75 ± 0.36*	3.70 ± 0.39
Rod neutrophils	%	0.38 ± 0.06	0.50 ± 0.10	0.13 ± 0.03	0.58 ± 0.10
	×10 ⁹ /L	0.014 ± 0.003	0.010 ± 0.002	0.003 ± 0.0001	0.020 ± 0.003
Segmented neutrophils	%	20.75 ± 3.07	16.25 ± 3.75	23.50 ± 3.38	15.50 ± 1.80
	×10 ⁹ /L	0.887 ± 0.082	0.377 ± 0.043*	0.585 ± 0.081	0.580 ± 0.087
Eosinophils	%	4.44 ± 0.54	4.00 ± 0.70	5.25 ± 0.93	3.58 ± 0.55
	×10 ⁹ /L	0.166 ± 0.036	0.096 ± 0.014	0.163 ± 0.037	0.131 ± 0.030
Monocytes	%	5.25 ± 0.97	2.00 ± 0.07*	3.00 ± 0.34	2.00 ± 0.37*
	×10 ⁹ /L	0.196 ± 0.025	0.056 ± 0.011*	0.082 ± 0.012*	0.185 ± 0.031
Lymphocytes	%	69.00 ± 3.44	77.00 ± 9.00	68.13 ± 4.49	78.25 ± 2.06*
	×10 ⁹ /L	2.962 ± 0.246	2.270 ± 0.270	1.917 ± 0.124*	3.215 ± 0.436
T-lymphocytes	%	6.63 ± 0.88	8.00 ± 1.00	8.50 ± 0.76	9.00 ± 0.20*
	×10 ⁹ /L	0.25 ± 0.03	0.19 ± 0.04	0.16 ± 0.03	0.26 ± 0.05

Notes: 1.*The difference is significant compared with the values in the group of intact animals (I), P < 0.05; 2.** The difference is significant in comparison with the values in the control (II) group of animals, P < 0.05.

The introduction of preparations based on phospholipids of both plant and animal origin did not significantly affect the number of lymphocytes in sick mice compared to the control group of animals (without treatment). At the same time, the introduction of dietary supplements "FLP-MD" into the body of sick animals increased the relative number of these cells by 1.4 times, and the use of essentielle-forte resulted in a decrease in the absolute number of lymphocytes (by 35%) compared to the animals of the intact group. At the same time, the number of T-lymphocytes in the blood significantly increased 1.4 times in comparison with intact animals only in group IV mice.

So, the modeling of gastroenteropathology in CBA mice is associated with a decrease in the peripheral blood ESR value and the number of leukocytes, mainly due to segmented neutrophils and monocytes. The correction of structural and functional disorders of the epithelial cells of the digestive tract with the use of dietary supplements "FLP-MD", in contrast to the drug essentielle-forte, was accompanied by an increase in the relative number of lymphocytes, a decrease in the peripheral blood hemoglobin content and an increase in ESR intensity, which occurred against the background of a tendency to increase the number of red blood cells.

As a result of the study of indicators of the general state of the organs of the immune system in experimental animals, it was found that the modeling of gastroenteropathology in mice (group II) is accompanied by a significant decrease in the mass of the thymus and spleen in comparison with intact

animals (Table 2). At the same time, the animals of this group showed a significant 45.5% decrease in the absolute number of lymphoid cells in the spleen as compared with the group of intact animals.

2. Indicators of the general state of the lymphoid organs of the immune system in experimental mice ($M \pm SD$, $n = 6-8$)

Index		Group of mice			
		I	II	III	IV
Thymus mass, mg		53.38 ± 4.38	$37.00 \pm 5.00^*$	48.25 ± 6.44	43.57 ± 6.61
Thymus index		2.26 ± 0.32	1.55 ± 0.35	2.09 ± 0.18	2.11 ± 0.35
Spleen weight, mg		110.38 ± 5.05	$78.00 \pm 8.00^*$	97.50 ± 9.08	121.29 ± 16.44
Splenic index		4.65 ± 0.31	3.50 ± 0.59	4.00 ± 0.40	5.61 ± 0.85
The number of lymphoid cells in the thymus	$\times 10^6$	47.88 ± 8.37	56.00 ± 7.09	53.63 ± 9.97	59.13 ± 6.46
	$10^6/\text{mg}$	0.533 ± 0.098	0.709 ± 0.060	0.612 ± 0.061	0.590 ± 0.092
The number of lymphoid cells in the spleen	$\times 10^6$	178.75 ± 17.00	$97.50 \pm 16.50^*$	163.75 ± 18.15	$233.75 \pm 19.05^{*,**}$
	$10^6/\text{mg}$	1.70 ± 0.04	1.19 ± 0.26	1.66 ± 0.34	2.24 ± 0.39

Notes: 1.*The difference is significant compared with the values in the group of intact animals (I), $P < 0.05$; 2.** The difference is significant in comparison with the values in the control (II) group of animals, $P < 0.05$.

The use of essentielle-forte and the "FLP-MD" dietary supplement is accompanied by the restoration of these indicators to the level of intact animals and did not significantly affect other indicators of the general state of the immune system organs, with the exception of the possible increase in the number of lymphoid cells in the spleen in animals of group IV compared to animals control and intact groups, respectively, by 2.4 and 1.3 times.

The results of the study of the endocrine function of the thymus indicate its significant inhibition in the process of modeling gastroenteropathology in laboratory mice. The use of essentielle-Forte in sick animals is accompanied by a significant increase in the endocrine function of the thymus, as a result of which the TSF level increases by 3.0 times, and the administration of dietary supplement "FLP-MD" to sick mice suppresses it (the TSF level decreases 2.0 times) relative to group II mice. The latter probably occurs due to the development of a stress reaction (immobilization stress), which can be caused by four times a day administration of dietary supplements (as opposed to a single use of essentielle-forte), since it is known that activation of the glucocorticoid function of the adrenal cortex is accompanied by inhibition of endocrine function. thymus [8], and with it the function of T-lymphocytes, which are a target for hormone antagonists.

Physiological death of lymphoid cells in the organs of immunity occurs through apoptosis (Nicoletti, 1991). However, a high degree of cell death, including in the thymus, is compensated by intense proliferation. It is she who determines the filling of the organs of the immune system with cells. Thus, the combination of the processes of proliferation and apoptosis of cells of the immune system is an important means of selecting their clones and is the basis for controlling the regularity of differentiation of T- and B-lymphocytes, the formation of an immune response and the implementation of the body's immunological defense (Udut et al., 2013).

The study of the processes of proliferation and apoptosis of lymphoid cells of the thymus and spleen of mice of different groups showed that during self-rehabilitation (group II) in mice, the processes of programmed death and proliferation of these cells are somewhat slowed down (Table 3).

3. The level of spontaneous and PHA-induced apoptosis and proliferation of lymphoid cells of the central organs of immunity in experimental CBA mice, % ($M \pm SD$, $n = 6-8$)

Index	Group of mice
-------	---------------

		I (control)	II	III	IV
Splenocytes	Apoptosis	2.20 ± 0.36	0.57 ± 0.19*	0.72 ± 0.16*	0.70 ± 0.15*
	Proliferation	17.15 ± 1.18	15.10 ± 2.03	18.74 ± 2.40	26.38 ± 3.75***
	IPA	7.80 ± 1.07	26.49 ± 1.38*	26.03 ± 1.32*	37.69 ± 1.71***
Thymocytes	Apoptosis	1.70 ± 0.40	0.98 ± 0.05	1.09 ± 0.22	1.18 ± 0.18
	Proliferation	29.03 ± 1.09	25.46 ± 0.65*	28.84 ± 0.89**	30.22 ± 1.04**
	IPA	17.08 ± 2.69	25.98 ± 1.82*	26.46 ± 2.54*	25.61 ± 2.03*
Splenocytes + PHA	Apoptosis	69.90 ± 5.19	71.04 ± 1.60	72.24 ± 2.95	72.89 ± 5.69
	Proliferation	38.59 ± 2.79	33.25 ± 2.16	35.26 ± 4.00	44.22 ± 2.13**
	IPA	0.55 ± 0.08	0.47 ± 0.02	0.49 ± 0.09	0.61 ± 0.06**
Thymocytes + PHA	Apoptosis	49.60 ± 4.16	45.08 ± 2.33	39.78 ± 2.04	42.17 ± 3.70
	Proliferation	28.73 ± 3.36	19.87 ± 2.80	19.86 ± 1.34*	24.55 ± 3.15
	IPA	0.58 ± 0.08	0.44 ± 0.02	0.50 ± 0.04	0.58 ± 0.09

Notes: 1.*The difference is significant compared with the values in the group of intact animals (I), $P < 0.05$; 2. ** The difference is significant in comparison with the values in the control (II) group of animals, $P < 0.05$.

Thus, the level of spontaneous proliferation of splenocytes and thymocytes in mice of the control group is equivalently reduced by 1.1 times compared with the group of intact animals. Correction with both *essentiale-forte* and "FLP-MD" dietary supplement does not significantly affect the intensity of apoptosis, but stimulates proliferative processes in the lymphoid cells of the thymus and spleen, which is especially pronounced in animals of group IV (the intensity of proliferation of splenocytes and 1.1 times thymocytes compared to control). The IPA value also undergoes corresponding changes in animals of group IV, namely: in the spleen it increases 4.8 times compared with the group of intact animals and 1.4 times in relation to the control group (on self-rehabilitation), and in the case of the thymus it increases 1.5 times relative to its values in the group of intact animals.

Thus, the ratio of proliferation and apoptosis processes is an important indicator of the functional state of the body's immune system. The use of corrective therapy in the form of dietary supplements "FLP-MD" causes the activation of proliferative processes in the organs of the immune system, especially in the spleen.

In addition, the results of microscopic studies indicate that guttalex in combination with diclofenac causes changes mainly in the stomach and depending on the sex of animals: in males, necrosis of the mucous membrane, and in females, dystrophic changes (vacuolar dystrophy) of epithelial cells in the glands of the cardiac region predominate. These drugs cause an active reaction of lymphoblasts and the differentiation of the latter into plasma cells, which indicates the presence of antigenic factors in the body of these animals. The use of *essentiale-forte* as a corrective therapy leads to active proliferation of epithelial cells in the glands of the stomach and hyperplasia of smooth muscle nuclei in males.

After the use of dietary supplements "FLP-MD" only in the esophagus of males there are dystrophic changes in the nuclei of squamous epithelium, while no morphological changes were revealed in the stomach. In females, the introduction of dietary supplements "FLP-MD" promotes the unresponsiveness of the cells of the basal layer in the esophagus (absence of mitosis), parenchymal degeneration of epithelial cells of the mucous membrane of the cardiac part of the stomach and active reaction of lymphoblasts and plasma cells in the submucosal layer. In intact animals, the reaction of cricokaryocytes predominates in the axillary layer, which indicates irritation of the surface epithelium by factors of unknown etiology.

Conclusion and future perspectives

As a result of the reproduction of an acute form of hemorrhagic gastroenteritis with diarrheal syndrome in CBA mice, the development of clinical symptoms of gastroenteropathology was established, which appeared from the first day of the experiment. In particular, this is a decrease in the mobility of animals, suppression of their general condition, exhaustion and loss of appetite, rarefaction of feces and a high percentage of mortality (up to 84%). Disappearance of clinical symptoms of experimental pathology in animals in self-rehabilitation is noted only on the 30th day of observation. They are also characterized by a decrease in the peripheral blood ESR value and leukopenia, mainly due to segmented neutrophils and monocytes. In these animals, a significant decrease in the mass of the thymus and spleen and the absolute number of lymphoid cells in the latter, a significant suppression of the endocrine function of the thymus, was established. In sick mice, the processes of programmed death and proliferation of lymphoid cells are somewhat slowed down. In addition, the results of microscopic studies indicate characteristic changes in the stomach and their dependence on the sex of animals: in males, necrosis of the mucous membrane, and in females, dystrophic changes (vacuolar dystrophy) of epithelial cells in the glands of the cardiac section predominate.

At the same time, the use of reparative therapy agents based on phospholipids of various origins in sick animals produces a pronounced reparative effect. At the same time, the effect of dietary supplements "FLP-MD" is not inferior to the drug *essentiale-forte*. Of the peculiarities of the effect, the introduction of bioadditives into the organism of sick mice deserves attention, the reparative properties are better expressed: a significant acceleration of the restoration of the mass of lymphoid organs; a significant increase in the relative number of T-lymphocytes in the peripheral blood (1.4 times) due to the activation of proliferative processes in the organs of the immune system (the proliferative activity of the thymus increases 1.5 times, and the spleen 4.8 times in comparison with intact animals), as well as a decrease in the time for restoration of the general clinical state of animals (on the 8-10th day from the beginning of the introduction of the supplement into the body versus the 10-12th day when using the drug *essentiale-forte*). Regularities have been established regarding the peculiarities of the effect of phospholipid-containing remedies of corrective therapy of various origins on the organism of laboratory animals with experimental gastroenteropathology, it is recommended to take into account when developing new drugs and appropriate treatment regimens for patients.

References

- Abdel Khalek, R. El-sheikh, Hayam, M. Samy Morsy, Tarek, H. Allam Abbas, & Wafaa, M. Abdelrazik (2012). Clinical and laboratory examinations of diarrhea and dehydration in newborn friesian calves with special reference to therapy with hypertonic and isotonic solution. *Life Science Journal-acta Zhengzhou University Overseas Edition*, 9(4), 181-184.
- Bach, J., & Dardenne, M. (1973). Studies on thymus products. II. Demonstration and characterization of a circulating thymic hormone. *Immunology*, 25, 353-362.
- Bothra, A., Arumugam, P., Panchal, V., Menon, D., Srivastava, S., Shankaran, D., Nandy, A., Jaisinghani, N., Singh, A., Gokhale, R. S., Gandotra S., & Rao V. (2018). Phospholipid homeostasis, membrane tenacity and survival of Mtb in lipid rich conditions is determined by MmpL11 function. *Scientific Reports*, 8(8317), 1-14. doi:10.1038/s41598-018-26710-z
- Colombo, S., Melo, T., Martinez-Lopez, M., Carrasco, M. J., Domingues, P., Pérez-Sala, D., & Domingues, R. (2018). P-150 - Phospholipidome of endothelial cells shows a different adaptation response upon oxidative, glycativ or carbonyl stress. *Free Radical Biology and Medicine*, 120(1), S90. doi: 10.1016/j.freeradbiomed.2018.04.297
- Deng, X., Tolstanova, G., Khomenko, T., Chen, L., Tarnawski, A., and Szabo, S., & Sandor, Z. (2009). Mesalamine restores angiogenic balance in experimental ulcerative colitis by reducing expression of endostatin and angiostatin: novel molecular mechanism for therapeutic action of mesalamine. *Journal of Pharmacology and Experimental Therapeutics* December, 331(3), 1071-1078. doi: 10.1124/jpet.109.158022
- Gryshchenko, V. A. (2020). Influence of phospholipid-containing additives on the functional condition of organs and systems of mice. *Ukrainian Journal of Veterinary Sciences*, 11(3), 14–23. doi: 10.31548/ujvs2020.03.002
- Gryshchenko, V. A., Sysolyatin, S. V., & Gulevata, J. V. (2018). Phospholipid composition of blood plasma and internal organs of rats with diclofenac-induced hepatitis. *Ukrainian Journal of Ecology*, 8(3), 211–215.
- Harvey, M., & Cave, G. (2014). Co-administration of phospholipid emulsion with first dose

bacteriocidal antibiotic may retard progression of the sepsis response in gram negative septicaemia. *Medical Hypotheses*, 50(4), 303-309. doi: 10.1016/j.mehy.2014.08.024

Leskova, G. F., Kaplun, A. P., Bezrukov, D. A., & Lvovsky, A. I. (2020). Influence of phosphatidylcholine nanosomes on phospholipid composition in liver cell plasma membranes and blood serum at experimental atherosclerosis. *Byulleten' Eksperimental'noj Biologii i Medicyny*, 170(2), 143-147. DOI: 10.1007/s10517-020-05028-9

Melnychuk, D. O., Gryshchenko, V. A., & Lytvynenko, O. N.: *Veterynarna biologichno aktyvna dobavka liposomal'noi' formy ta sposib reparatyvnoi' terapii' v gepatologii'* [Veterinary biologically active additive of liposomal form and method of reparative therapy in hepatology]. Patent UA, 86516 (2009). (in Ukrainian).

Melnychuk, D. O., Gryshchenko, V. A., Tereshchenko, S. V., & Ribova, Z. B.: *Sposib modeliuvannia medykamentoznoho hastroenterytu z vyrazkovo-eroziinym protsesom u laboratornykh shchuriv* [Method for modeling gastroenteritis with ulcerative-erosive process in laboratory rats]. Patent UA, 83904 (2008). (in Ukrainian)

Moorhead, P. S., Nowele, P. C., Mellman, W. J., & Battips, D. M. (1960). Chromosome preparations of leucocytes cultured from human peripheral blood. *Experimental Cell Research*, 20(3), 613-6. doi: 10.1016/0014-4827(60)90138-5

Nicoletti, I., Migliorati, G., Pagliacci, M. C., Grignani, F., & Riccardi, C. (1991). Grignani A rapid and simple method for measuring thymocyte apoptosis by propidium iodide staining and flow cytometry. *Journal of Immunological Methods*, 139(2), 271-279. doi: 10.1016/0022-1759(91)90198-0

Qingbiao, Xu, Yueming, Wu, Hongyun, Liu, Yingming, Xie, Xinbei, Huang, & Jianxin, Liu (2014). Establishment and characterization of an omasal epithelial cell model derived from dairy calves for the study of small peptide absorption. *Plos One*, 9(3), e88993. doi: 10.1371/journal.pone.0088993

Sato, H. (2010). Fecal trimethylamine, lactate and volatile fatty acid concentrations and their relationships with diarrhea in newborn dairy calves. *Journal of Veterinary Medical Science*, 72(12), 1551-1555. doi: 10.1292/jvms.10-0162

Solís-Calero, C., Ortega-Castro, J., Frau, J., & Muñoz, F. (2015). Nonenzymatic reactions above phospholipid surfaces of biological membranes: reactivity of phospholipids and their oxidation derivatives. *Oxidative Medicine and Cellular Longevity*, 319505. doi: 10.1155/2015/319505

Szabo, S., Deng, X., Khomenko, T., Chen, L., Tolstanova, G., Osapay, K., Sandor, Z., & Xiong, X. (2007). New molecular mechanisms of duodenal ulceration. *Annals of the New York Academy of Sciences?* 1113, 238-255. doi: 10.1196/annals.1391.033

Tomchuk, V., Gryshchenko, V., Tsvilikhovskiy V., & Illek J. (2019). Enterocytes membranes of the small intestine at pathology and conditions of hibernation. Czech Republic: University of Veterinary and Pharma-ceutical Sciences in Brno.

Tomchuk V., Gryshchenko, V., Vlizlo, V., & Enciu V. (2019). Corrective effect of milk phospholipids in pathological conditions. *Iași Editura Ion Ionescu de la Brad*.

Udud, V. V., Vengerovsky, A. I., & Dygai, A. M. (2013). Effects of phospholipid hepatoprotectors on apoptosis during experimental liver pathology induced by isoniazid and paracetamol. *Bulletin of Experimental Biology and Medicine*, 154(5):614-617. doi: 10.1007/s10517-013-2012-9

Yang, K. J., Son, J., Jung, S. Y., Yi, G., Yoo, J., Kim, D. K., & Koo, H. (2018). Optimized phospholipid-based nanoparticles for inner ear drug delivery and therapy. *Biomaterials*, 171(7), 133-143. doi: 10.1016/j.biomaterials.2018.04.038

Zhang, X., Yang, L., Liu, Y., Song, Z., Zhao, J., Chen, D., Yu, H., Li, R., Wang, Y., Yang, K., Chen, Y., Xia, M., & Zhang, L. W. (2018). Detection of nanocarrier potentiation on drug induced phospholipidosis in cultured cells and primary hepatocyte spheroids by high content imaging and analysis. *Toxicology and Applied Pharmacology*, 348, 54-66. doi: 10.1016/j.taap.2018.04.016

Грищенко В. А., Іллек Й., Томчук В. А. (2021). Клінічна ефективність фосфоліпідовмісних препаратів різного походження за експериментальної гастроентеропатології мишей. *Ukrainian Journal of Veterinary Sciences. Хвороби органів травної системи є надзвичайно поширеними серед тварин, особливо в молодняка. Мета цієї роботи полягала у визначенні особливостей корегувальної ефективності засобів репаративної дії на основі фосфоліпідів різного походження за результатами комплексного дослідження клінічних, гематологічних, імунологічних показників та структурно-функціонального стану імунокомпетентних органів у мишей лінії СВА за експериментальної гастроентеропатології.*

В результаті відтворення гострої форми геморагічного гастроентериту з діарейним

синдромом у мишей лінії СВА відмічали розвиток характерних клінічних симптомів. Незалежно від природи походження фосфоліпідів, препарати на їх основі виявляли виражений репаративний ефект дії щодо ушкоджених клітин. При цьому, ефективність біодобавки «FLP-MD» на основі фосфоліпідів з молока за окремими показниками виявлялася кращою порівняно з препаратом есенціале-форте на основі фосфоліпідів із сої. Так, особливістю впливу біодобавки «FLP-MD» на організм хворих мишей є пришвидшення відновлення загального клінічного стану тварин (на 8–10-ту добу від початку введення в організм біодобавки проти 10–12-ої доби при застосуванні препарату есенціале-форте), відновлення маси лімфоїдних органів (тимусу і селезінки); збільшення відносної кількості Т-лімфоцитів у крові в 1,4 раза за рахунок активації проліферативних процесів в органах імунної системи (в селезінці у 4,8 раза, в тимусі у 1,5 раза).

Ключові слова: експериментальна гастроентеропатологія, лабораторні миші лінії СВА, клінічні, гематологічні, імунологічні, мікроскопічні дослідження, фосфоліпідиди з молока і сої, корегувальна ефективність.

**MODERN STRATEGY, NEW METHODS AND MEANS FOR CONTROL OF
HELMINTHIASES IN UZBEKISTAN**

A. O. ORIPOV¹, Doctor of Veterinary Sciences, Professor

E-mail: uzniv@mail.ru

N. E. YULDASHEV², Doctor of Veterinary Sciences, Senior Research Fellow,
State Scientific Center for the Circulation of Veterinary Medicines and Feed Additives

E-mail: gnkc@vetgov.uz

¹*Scientific Research Institute of Veterinary Medicine of the Republic of Uzbekistan, 35 A. Beruniy st., village Taylyak, Taylyak district, Samarkand region, Republic of Uzbekistan*

²*State Committee for Veterinary Medicine and Livestock Development of the Republic of Uzbekistan, 100 Didor st. Chilanzar district, Tashkent, Republic of Uzbekistan*

Abstract. *The modern strategy to control the main, widespread helminthiases of farm animals provides for a complex of anthelmintic measures, including planned therapeutic and preventive deworming based on data from the study of the epizootology of helminthiases in each specific climatic-geographical zone; the implementation of measures for the pasture prevention of geohelminthiases and the control of the main, intermediate, and additional hosts for causative agents of biohelminthiases, including zoonotic helminthiases (echinococcosis, coenurosis, and cysticercosis); the implementation of measures for chemoprophylaxis of helminthiases in certain branches of animal husbandry, for example, in sheep breeding; by using anthelmintic-salt mixtures; the use of agents that increase the immunobiological protective properties of the animal body against helminthiases and other diseases through the widespread use of vitamins, micro- and macroelements and other biological stimulants.*

Keywords: *helminths, helminthiases, deworming, molluscicides, anthelmintics, anthelmintic-salt mixtures, immunostimulants*

Introduction

It is known that the control of animal helminthiases includes the following main measures: planned therapeutic and preventive deworming, the volume (multiplicity) and terms of which is based on the pathogen biology and epizootology of parasitic infections; prevention of animal infestation with pathogens of helminthiases based on the neutralization (disinfection) of the external environment in relation to geohelminthiases (soil-transmitted helminthiases) and the control of intermediate and additional hosts of pathogens of many biohelminthiases, as well as measures aimed at preventing infestation of productive animals with pathogens of larval cestodiasis (echinococcosis, coenurosis, and cysticercosis); chemoprophylaxis and measures that increase the general immunobiological resistance of the animal body to helminthiases and other diseases.

Analysis of recent research and publications

Livestock productivity depends on many factors, such as animal feeding, keeping, and health. Among the animal health problems, parasitic diseases constitute a significant part. Livestock are parasitized by various helminth species, the most important being gastrointestinal nematodes, lungworms, and liver fluke. These pathogens can cause severe disease, affect productivity in all classes of stock, and are amongst the most important production-limiting diseases of grazing ruminants. Essentially all herds/flocks in a grass-based production system are affected. Infections with gastrointestinal nematodes and liver fluke are more chronic and the major economic impact is due to sub-clinical infections causing reduced growth, milk yield, and fertility. Infections with lungworm are more acute and can place a sudden high economic burden on a farm due to mortalities and sharp decreases in milk yield (Charlier et al., 2015).

The economic burden of helminthiases for the livestock industry is quite high. For example, in 2020, Charlier et al. conducted an assessment of the economic burden of 3 major parasitic helminth infections (gastrointestinal nematodes, *Fasciola hepatica*, and *Dictyocaulus viviparus*) to the ruminant livestock industry in Europe. The economic impact of these parasitic helminth infections was estimated by a deterministic spreadsheet model as a function of the proportion of the ruminant population exposed to grazing, the infection frequency and intensity, the effect of the infection on animal productivity and mortality and anthelmintic treatment costs. Also, they estimated the costs of anthelmintic resistant nematode infections and collected information on public research budgets addressing helminth infections in ruminant livestock. According to their data, the combined annual cost of the three helminth infections in 18 participating countries was estimated at € 1.8 billion. Eighty-one percent of this cost was due to lost production and 19 % was attributed to treatment

costs. The cost of gastrointestinal nematode infections with resistance against macrocyclic lactones was estimated to be € 38 million annually. The annual estimated costs of helminth infections per sector were € 941 million in dairy cattle, € 423 million in beef cattle, € 151 million in dairy sheep, € 206 million in meat sheep and € 86 million in dairy goats (Charlier et al., 2020).

The impact of the helminth infections could be understood from the fact that treatment of lactating animals with anthelmintic drugs resulted in an increase of 4–18% in milk production. The liver flukes and amphistome parasites are responsible for decreased productivity through stunted growth, reduced fertility, and diminishing the quality as well as quantity of milk and meat. The amphistomes along with gastrointestinal nematodes could be responsible for a significant reduction (approximately 0.4–3.0 L/day) in milk production in cows. The production losses are not the sole source of economic losses rather the cost of treatment also contributes a major chunk to the overall losses incurred to the global livestock industry (Rehman & Abidi, 2021).

The treatment and prevention of helminthiasis in farm animals is not only important for the productivity of animal husbandry but also have a crucial value for human health. It is well known that several helminth infections are common for both animals and human. Helminth zoonoses are parasitic infections that can be shared by animals and humans (Arias et al., 2013). Various parasites infecting humans depend on vertebrate animals to complete their life cycle. Humans most commonly become infected with these zoonotic parasites through the consumption of infected hosts or through fecal-oral contamination. The results of these infections may vary from asymptomatic carriership to long-term morbidity and even death. Although data are still scarce, it is clear that these parasitic zoonoses present a significant burden for public health. Moreover, parasitic zoonoses can lead to significant economic losses, both directly, through their adverse effects on human and animal health, and indirectly, through control measures required in the food production chain (Devleeschauwer et al., 2014).

Nowadays, one of the most prevalent zoonotic diseases is infection with helminth parasites, which infect about one-third of the human population worldwide (Reda, 2018). Such widespread epidemiology of these infections can be attributed to a range of human factors including social and dietary changes as well as increased mobility of the human population. As human population grows, the demand for food products with a high protein content increases under intensive farming, which is inevitably leading to a greater spread of animal diseases and their transmission to humans. Some of the most important and well-known human zoonoses are caused by worm or helminth parasites, including species of nematodes (trichinellosis), cestodes (cysticercosis, echinococcosis), and trematodes (schistosomiasis) (Robinson & Dalton, 2009).

The extraordinary prevalence of helminth infections undoubtedly reflects their ability to manipulate the host immune system, suppressing responses that could result in their ejection. Host immunity has also developed (over eons of coevolution with parasites) mechanisms to limit pathology and to best balance susceptibility, resistance, and immune pathogenesis. Hence, immune responses often permit ongoing infection in preference to complete parasite elimination and the collateral damage that would result. In other cases, this balance is upset, and immune dysregulation and pathology ensue (McSorley & Maizels, 2012).

Many of the parasitic worms have complex multistage life cycles that involve several hosts. Within their mammalian hosts, they often undergo extensive growth and differentiation with the ultimate goal of producing stages intended for transmission to the next intermediate host. Usually, the life stage responsible for infecting the mammalian host is the larva, and the larva must migrate within the host to its appropriate niche where it can grow and reproduce. Since the offspring are intended for transmission to another animal, they must necessarily be capable in some way of entering a site from which they can leave the host. How all this is accomplished varies from one helminth to another. Nevertheless, despite this extensive organismal complexity, in the majority of cases the immune responses of the hosts to worm infection are remarkably similar (MacDonald et al., 2002).

Whenever parasitic worms such as platyhelminths (flatworms) and nematodes (roundworms) invade their host, there is a need for hemostasis and outwitting host immune defenses and expulsion mechanisms. The helminth produces excretory-secretory antigens which mediate a protein-protein interaction in the extracellular ambience with either the fluid phase or host receptor cells. Excretory-secretory antigen production is not to overtake the immune system but to modulate and manipulate the immunity of the host to their own favor. The autonomous immune system of the host, on the other hand, respond to the invasion of the parasite by inducing the production and mobilization of certain proteins such as; cytokines (interleukin-13, interleukin-10, interleukin-5, and interleukin-4), non-specific immunoglobulin E, parasite-specific immunoglobulin, mobilization of mast cells, basophils and eosinophils. These collections of responses to helminths are known as the T-helper-2 (Th2) immune response (Idris et al., 2019).

In many chronic helminth infections, however, the protective type 2 response appears to be restrained by the body's own immunosuppressive mechanisms, such as regulatory T cells and the down-modulatory cytokines they produce, which results in ineffective and unresponsive immune cell populations that cannot eliminate the parasite. The ability of helminth parasites to promote host regulatory pathways to block Th2 immunity is equally apparent in human and animal infections, presenting in both settings a shared challenge of directing new vaccines to select protective and not counter-productive components of the immune system. One consequence of the immunoregulatory nature of helminth parasites is that most individuals fail to develop protective immunity to infection, despite frequent exposure to infective stage parasites. Even following curative drug treatment, subjects show little resistance to rapid reinfection with soil-transmitted nematodes that establish in the intestinal tract (Hewitson & Maizels, 2014).

Despite significant advances in parasite immunology research, challenges remain in understanding how precisely helminths interact with their hosts and tolerate the complex immune responses generated against them, and how to use such knowledge to develop new ways of combating these parasitic infections (Foster & Elsheikha, 2012).

Control of helminth parasites is a key challenge for human and veterinary medicine. Although there are many different approaches to the control of helminth parasitism in livestock, including nutritional, immunological, and biological interventions, at present, effective control relies almost exclusively on effective synthetic anthelmintic drugs (Tsotetsi et al., 2013; Kotze et al., 2020; Nixon et al., 2020). Most of these compounds have broad-spectrum activity, but effective control ultimately relies on multiple treatments each year (Morgan et al., 2013). In some cases, organic farming, for instance, plant-derived or homeopathic preparations are preferred to synthetic drugs. Commercial plant preparations only show an anthelmintic activity in only a very few cases, and up to now, they have not proven their efficacy. Homeopathic drugs are not claimed as having an anthelmintic efficacy but rather promote the resilience of hosts to infections (Cabaret et al., 2002).

Anthelmintics were primarily generated for the treatment of veterinary parasites, and their application has then been expanded for the treatment of human patients. They have a variety of chemical entities and act through several modes of action (Alavi & Shahmabadi, 2021). The mode of action of most anthelmintic drugs depends on the affinity of the parasite's signal protein, anion and cation channels and neuromuscular receptors to the drug. The drug binds to these sites and causes instability, spastic paralysis, or the death of the parasite (Idris et al., 2019).

According to chemical structures and pharmacological properties, there are seven classes of modern anthelmintics, including benzimidazoles, probenzimidazoles, tetrahydropyrimidines, imidazothiazoles, isoquinolines, salicylanilides, and macrocyclic lactones. The pharmacokinetics of anthelmintics, including their absorption, distribution, and biotransformation/elimination pattern, are critical factors, which determine the time to a maximum effect-site concentration of the drugs in the body. Anthelmintics are administered by oral drench (as a general route), slow-release bolus, injection, or in-feed. Drug entrance and accumulation into a parasitic worm are crucial factors to achieve the optimal therapeutic outcome. Also, other factors, such as i) the balance among drug entry, ii) the capacity of the parasite to metabolize and inactivate the drug, and iii) the drug efflux capacity of the parasite, determine the drug accumulation within a parasite. The exposure time of parasite to active drug concentrations is a critical factor that affects the efficacy and/ or durability of activity of most anthelmintics used in ruminants. Overall, these factors are responsible to determine the ultimate anthelmintic activity (Alavi & Shahmabadi, 2021).

Despite the extraordinary success in the development of anthelmintics in the latter part of the last century, helminth parasites of domestic ruminants continue to pose the greatest infectious disease problem in grazing livestock systems worldwide. Newly emerged threats to continuing successful livestock production, particularly with small ruminants, are the failure of this chemotherapeutic arsenal due to the widespread development of anthelmintic resistance at a time when the likelihood of new products becoming commercially available seems more remote. In the context of helminth control in ruminant livestock, the mindset of 'suppression' needs to be replaced by 'management' of parasites to maintain long-term profitable livestock production. Existing effective chemical groups need to be carefully husbanded and non-chemotherapeutic methods of parasite control need to be further researched and adopted, if and when, they become commercially available (Waller, 2006).

When first introduced, all anthelmintic drugs are highly efficacious, but frequent and widespread use and misuse has resulted in the emergence of resistant parasite populations, such that anthelmintic resistance is now a major global problem and is the greatest threat to the sustainable control of helminthiasis in the short to medium term (Morgan et al., 2013). The impact of this has been particularly severe in the livestock industries, with significant levels of resistance worldwide in gastrointestinal nematodes of sheep, goats, and

cattle. Resistance to anthelmintics is also widespread in gastrointestinal parasites of horses and canines. Minimizing the impact of drug resistance requires an ability to detect its presence. This allows for drug-use decisions to be made based on the knowledge of what drugs remain effective against the target helminth population. Once resistance has been detected to a particular drug or drug class, the use of alternative drugs ensures that parasitic infections can be effectively controlled and that further selection pressure is not applied by the drug for which resistance is emerging (Kotze et al., 2020).

Risk factors for anthelmintic resistance development include parasite biology and epidemiology, the dynamics of the host-parasite relationship, treatment frequency, treatment strategies that result in various levels of refugia and differences in anthelmintic pharmacokinetics between host species. Preserving “refugia” (the proportion of populations of parasites not exposed to anthelmintics) is the current goal of parasite control in small ruminants and horses and has been deemed the single most important factor involved in the selection of anthelmintic resistance parasites. A selective approach to deworming is currently recommended in veterinary medicine in order to preserve refugia and slow anthelmintic resistance. Animals in the herd that are the least clinically affected based on fecal egg counts are left untreated. Anthelmintics are then administered to the most affected when there are more eggs and larvae on the pasture so the presence of susceptible parasite populations on pasture will “dilute” the resistant populations and thereby preserve refugia (Tinkler, 2020).

The eradication of helminth infections remains a distant goal, due to a lack of effective vaccines, limited pharmacological efficacy, emerging drug resistance, and rapid reinfection in environments where the transmission cannot be interrupted (McSorley & Maizels, 2012). This requires the development of alternative treatment approaches and drugs for the control of helminths (Reda, 2018; Idris et al., 2019).

The resistance of helminths to drugs over the years generated a hypothesis on whether preventive chemotherapy could be used against helminthiasis. Currently, the work on the development of prophylactic vaccines (as an alternative to anthelmintics) is carried out and there are some successful attempts. For livestock, a subunit vaccine called Barbervax, developed in Australia, has been commercialized for *Haemonchus contortus* that consists of a complex combination of native antigens from the worm’s gut. Barbervax is about 70% effective at reducing worm burdens and about 90% effective at reducing the number of eggs in the feces, which greatly reduces egg numbers throughout the pasture, and thus, the number of infections later on (Noon & Aroian, 2017). The vaccines for trichuriasis and ascariasis are currently undergoing preclinical testing. Hookworm, schistosomiasis, onchocerciasis and other soil-transmitted helminthiasis vaccines are in various stages of development (Idris et al, 2019). However, the development of vaccines against parasitic infections often is quite complicated due to challenges in their manufacturing, preclinical and clinical research.

The control of helminthiasis in farm animals is a global challenge considering the high prevalence of helminth infections and significant economic losses from these diseases. In every country all over the world, there is a distinct peculiarity in strategy to control and prevent helminthiasis in farm animals according to social, economic, geographic and other factors. This determines the purpose of our work – to study the modern strategy, new methods and means for control of helminthiasis in the Republic of Uzbekistan.

Materials and methods of researches

A systematic review of literature sources concerning methods and tools for control of helminthiasis was conducted. The methods of analysis and synthesis of scientific data were used. According to the main tasks of the article, the relevant scientific papers from the Republic of Uzbekistan were selected for review.

Results of the research and their discussion

Means and methods of planned deworming, in particular, anthelmintic drugs and methods of their application, as well as their effectiveness against different groups of helminthiasis – trematodiasis, cestodiasis, and nematodiasis are widely and comprehensively covered in fundamental works (Demidov & Potemkina, 1980; Demidov, 1982). Several studies have been carried out to improve methods of deworming (Dolnikov, 1956; Oripov & Petrosyan, 1974; Oripov, 1978; Oripov, 1978a; Oripov, 1980; Oripov, 1990) as well as searching for new anthelmintic drugs (Oripov et al., 2016^a; Oripov et al., 2016^b; Oripov et al., 2020).

An important part in the complex of measures to control helminthiasis, as is known, is the control of intermediate hosts of pathogens of biohelminthiasis. In particular, control of freshwater snails of the family *Lymnaeidae* and *Planorbidae* has important and sometimes crucial value for the prevention of widespread dangerous trematodiasis in farm animals, such as fasciolosis, schistosomiasis (orientobilharziasis), and paramphistomatosis (Mereminskii, 1967; Gorokhov, 1970; Zharikov, 1975; Yuldashev & Oripov, 2016), while it is important to control oribatid mites – intermediate hosts of the pathogens of cestodiasis for pasture prevention of anoplocephalatoses (monieziosis) (Kuznetsov, 1972).

Chemoprophylaxis of helminthiasis is of special importance in the control of helminthiasis. In this regard, the prevention of helminthiasis by free feeding of phenothiazine-salt, phenothiazine-copper-sulphate-salt, and phenothiazine-molybdenum-copper-sulphate-salt mixtures in the ratios of 1:9, 10:1:89, 10:1:1:88,

respectively, was developed in the middle of the last century (Boev & Redko, 1947; Irgashev, 1963; Irgashev, 1963^a; Irgashev, 1963^b).

It should be emphasized that the introduction of chemoprophylaxis into the veterinary practice for the control of helminthiasis with the use of phenothiazine-salt mixtures has led to a sharp decrease in the incidence of many helminthiasis in sheep and goats, especially bunostomosis, esophagostomosis, and chabertiosis, which are almost never found at the present, the infection with dictyocaulosis, gastrointestinal strongyloidiasis, and intestinal cestodiasis has also sharply decreased.

However, due to the cessation of phenothiazine production in Yekaterinburg in the 1980s as an environmentally harmful production, veterinary practice lost this means of preventing helminthiasis, i.e. phenothiazine.

Due to the above, we developed new anthelmintic-salt mixtures using modern anthelmintic agents instead of phenothiazine – albendazole, fenbendazole, and tetramisole (Oripov & Dzhabborov, 2000; Oripov & Dzhabborov, 2003), as well as anthelmintic-salt mixtures with bentonite (Amonov, 2008) and mixtures, enriched with trace elements taking into account the geochemical composition of the soil in individual regions (Yuldashev, 2018). These developments are recognized as inventions and the corresponding patents are received for them (UZ№IAP03349, UZ№IAP03350, and UZ№IAP03351).

Another system of measures aimed at reducing the infestation of productive animals with helminthiasis are measures aimed at increasing the body's resistance to helminthiasis. In this regard, deserves attention the work on the development of methods for the use of vitamins, trace elements, and other biologically active agents that stimulate the body's natural resistance to helminthiasis.

In this direction, the works of Akopian (1956), Davtian & Akopian (1958), Akopian (1960), Oripov (1990) are of interest, in which experimental data on the positive effect of vitamin A on the increase of resistance of sheep to fasciolosis and cystocaulosis are given. It has been established that infestation of sheep with these helminthiasis leads to a decrease in vitamin A content in the liver.

We also conducted research to determine the effect of micronutrients on the infestation of animals, in particular sheep, with helminthiasis, as well as the effect of a natural biostimulator, gossypin, on the infestation of chickens and sheep with helminthiasis and chicken productivity.

Directions, volume, and nature of our research in the above areas, analysis of the results are given below.

Analysis of the results of multi-year studies in the Republic of Uzbekistan (Badanin, 1949; Nepoklonov, 1959; Azimov, 1963; Irgashev, 1963; Sadykov, 1973; Azimov, 1974; Salimov, 1974; Oripov, 1983) shows that the main, according to the founder of helminthology in the Republic of Uzbekistan, Badanin, the "main" helminthiasis in the country: in sheep and goats – fasciolosis, dicrocoeliasis, larval cestodiasis (echinococcosis, coenurosis, and cysticercosis), anoplocephalatoses (monieziosis, avitellinosis, and tisaniesiosis), dictyocaulosis and gastrointestinal nematodosis (marshallagiosis, nematodiosis, ostertagiosis, etc.); in cattle – fasciolosis, dicrocoeliasis, larval cestodiasis, anoplocephalatoses and gastrointestinal strongyloidiasis; in pigs – ascariasis, oesophagostomosis, and triocephalosis; in birds (chickens) under floor housing – ascariasis and heterakidosis, and in some regions – raietiosis, capillariosis, prosthogonimosis, etc. It is also established that the main helminthiasis of horses in the Republic of Uzbekistan are strongylosis, strongyloidiasis, trichonematosis, and in some limited areas – anoplocephalatoses (Isaev, 2019).

For deworming of animals in the 60–70s of the last century, carbon tetrachloride, hexachlorparaxilolum, and hexichol were used, and later, in the 80–90s, dertilum (dertilum O for small ruminants and dertilum B for cattle) and analogs of this drug (bilevon, rafoxanide, etc.). Lugol's solution was widely used against dictyocaulosis, phenothiazine, nilverm (tetramisole), and salts of piperazine – against nematodosis, phenasalum, copper sulfate, bithionolum, dichlorophen, bunamidine, cetovex, droncit, lopatol, etc – against intestinal cestodiasis. Phenothiazine, piperazine, thiabendazole and, more recently, albendazole, fenbendazole, and tetramisole have been widely used against nematodosis (Demidov & Potemkina, 1980; Demidov, 1982).

These anthelmintic drugs were used mainly by individual deworming, i.e. were based on the administration of a certain dose of the drug to each animal individually. These methods, along with the positive qualities (accuracy of dosing based on individual indicators of the animal), have several disadvantages (requires a lot of time and labor, the possibility of injury to animals and veterinary staff) and is not always acceptable, i.e. when there is much livestock and insufficient labor force, individual deworming is difficult to carry out.

Given this situation, methods for group deworming of animals were developed – by free feeding of anthelmintic drugs in a mixture with feed (compound feed and bran), by free feeding of medicated feed pellets and briquettes (Oripov, 1978; Oripov, 1978^a; Oripov, 1978).

In addition to improving these methods, we have developed a group method of deworming sheep by administration of nilverm (tetramisole) with water *ad libitum* during drinking (Oripov & Petrosian, 1974). The

essence of this method is that the anthelmintic drug is dissolved in water intended for watering a certain group of animals (sheep and goats). To do this, it preliminarily determines the amount of water consumed by the sheep in the given conditions, which is achieved by conducting a control watering of a small group (10–15 sheep) of animals in these conditions. Then the tank is filled with water intended for watering the whole group (flock) and anthelmintic drug, in our example – nilverm (tetramisole), calculated for the whole group (flock). The anthelmintic drug is first dissolved in a small amount of water (in a bucket), which is mixed with the total volume of water (in the tank), intended for watering of all groups (flocks). Sheep are admitted to the watering hole in small groups of 50–100 animals, with the expectation that all sheep in this group have free access to the gutter where water from the tank enters.

This method has several advantages over individual deworming: it does not require much time and additional labor, eliminates injuries to animals, allows you to cover the entire livestock available on the farm, and in a short time to complete anthelmintic measures for health improvement of farms from helminthiasis.

However, anthelmintic drugs with relatively high toxicity cannot be used by this method, i.e., drugs used by group methods must have a therapeutic index of at least 5, i.e. therapeutic doses should be 5 times less than toxic.

Our method of group deworming of sheep by administration of anthelmintic drugs with water *ad libitum* is especially acceptable in the conditions of sheep farms located in the desert-pasture zone, where there are no open water sources and sheep go to the watering hole, which is carried out in specially equipped places. Such structures consist of deep wells, a water lift, a reservoir and a gutter for watering.

The method of group deworming of sheep with water developed by us was subjected to a commission inspection and approved by the Main Directorate of Veterinary Medicine of the Ministry of Agriculture and Food of the USSR in 1973 and accepted as an “Innovation Proposal”.

Another area of the development and improvement of deworming methods is the development of methods for the use of anthelmintic drugs in feed mixtures and medicated feed pellets (Oripov, 1978; Oripov, 1978^a; Oripov, 1978). The essence of these methods is to include a therapeutic dose of anthelmintic drugs in the composition of feed (compound feed, bran) or feeding them in the form of medicated feed pellets. We have developed and implemented in the practice to control gastrointestinal and pulmonary nematodes and anoplocephaloses feed mixture and medicated feed pellets with nilverm (tetramisole), phenasalum for sheep, piperazine, tetramisole, and albendazole for deworming of chickens under floor housing.

The second important link in the complex of measures to control helminthiasis, as is known, is measures aimed at preventing the infection of animals with helminthic pathogens in the environment – in pastures and livestock buildings.

Particularly important in this link is the infection of farm and wild animals with such very dangerous helminthiasis as fasciolosis, schistosomiasis (orientobilharziasis), paramphistomatosis (paramphistomosis, liorchosis, calicophorosis, gastrotiliariosis). The intermediate hosts for causative agents of these trematodiasis (genera *Fasciola*, *Schistosoma*, and family *Paramphistomatidae*) are freshwater snails of the genera *Lymnaea* and *Planorbis*.

Therefore, to prevent infection of productive animals with fasciolosis, schistosomiasis (orientobilharziasis) and paramphistomatosis, it is necessary to control freshwater snails – intermediate hosts of trematodes (fascioles, schistosomes, and paramphistomes), which is achieved by draining the habitats of these snails, breeding of waterfowl (ducks, geese) – biological enemies of these snails, and the most effective and reliable way – the use of molluscicides, i.e. chemicals.

As we know, large-scale and in-depth studies have been conducted to investigate molluscicides of chemical origin (Mereminskii, 1967; Gorokhov, 1970; Zharikov, 1975). However, the developed and proposed molluscicides are usually inaccessible, and some of them are toxic to animals and not environmentally friendly (5,4-dichlorosalicylanilide, copper sulfate, etc.).

In this regard, we have developed readily available molluscicides, some of which are widely used in agriculture as a mineral fertilizer, as well as in medical practice, and the food industry. In particular, we tested various concentrations (from 1:100 to 1:1000000) of these molluscicides in experiments conducted in the laboratory (in aquariums), as well as in natural habitats of snails (springs, ditches, coastal areas of canals, rivers, and lakes, etc.).

The research results made it possible to establish that mineral fertilizers – ammonium sulfate ($(\text{NH})_2\text{SO}_4$) and potassium chloride (KCl) at concentrations of 0.1% and 0.2%, respectively, lead to the death of snails in 24–72 hours, baking soda (sodium bicarbonate) at a concentration of 1:300–1:400, i.e. 0.3–0.4%, also exhibits a satisfactory molluscicidal effect, and hydrogen peroxide (H_2O_2) and potassium permanganate (KMnSO_4), at concentrations of 1:400000 and 1:400000, respectively, lead to 100% death of snails in 24 hours. Common table salt (NaCl) also has a certain molluscicidal effect: its concentration of 1:200–1:250 leads to the death of

snails in 24–72 hours (Yuldashev, 2020). The molluscicides recommended by us – ammonium sulfate, baking soda, hydrogen peroxide, and potassium permanganate were accepted as “Inventions” and patents were obtained (UZ№IAP05448, UZ№IAP05449, UZ№IAP05573, and UZ№IAP05802), and developed by us “Manuals” on the application of ammonium sulfate and potassium chloride are accepted for use (State Committee of the Republic of Uzbekistan for veterinary medicine and development of animal husbandry).

Of particular importance in the prevention of helminthiasis is the increase in the immunobiological defenses of the animal organism to these infections. Naturally, this is achieved by proper feeding and caring for animals, as well as by stimulating the natural defense mechanisms of the animal's body resistance to diseases through the use of immunostimulants, vitamins, enzymes, and micro- and macroelements (Daugalieva & Oripov, 1990).

In this regard, we, together with the staff of the Institute of Chemistry of Plant Substances of the Academy of Sciences of the Republic of Uzbekistan have developed a natural biostimulator – gossipren, obtained from the leaves of the cotton plant (*Gossypium hirsutum*), which contains a biologically active substance from the group of polyphenols that stimulates sexual function, in particular ovulation. In addition to polyphenols, which account for 4.3% of the composition of the preparation obtained from the extract of cotton plant leaves, gossipren contains about 30 chemical substances, including tocopherols (provitamin E), phytosterols (provitamin D), carotene (vitamin A coenzyme), ascorbic acid (vitamin C) and various trace elements, enzymes, and other biologically active elements.

The use of gossipren for 3 years in poultry farms of both industrial type with cage housing systems of chickens, and private households and farms with floor housing of chickens, showed that gossipren was fed to chickens from 1–1.5 months of age with feed (feed mixture consisting bran, crushed wheat, and corn, hay flour) in an amount of 0.1% of the feed volume, led to an increase in egg production by 38–51%, and the experimental pullets began to lay eggs 12–15 days earlier than their peers from the control (not receiving gossipren) group and eggs obtained from birds of the experimental group weighed 4–5% more than eggs obtained from birds of the control group (Oripov et al., 2016).

It was found that gossipren as an estrogenic agent, in addition to increasing the productivity of birds, has a noticeable effect on the helminthic situation in farms with floor keeping.

Thus, the average total intensity of the infection of chickens by different helminths (capillaries, raillietines, ascarides, heterakis) was 27.5 specimens in the experimental group, while in chickens of the control group that did not receive gossipren with food, an average of 151 specimens' helminths were found. Consequently, the intensity of infestation by helminths in chickens that received gossipren in the diet is about 5 times lower than in birds that did not receive this agent.

In the future, we plan to test this substance on animals, especially on multi-fetal animals – pigs, rabbits, as well as on sheep, in particular, on Karakul sheep.

Conclusions and future perspectives

It should be noted that helminths of farm animals are still often found and play a certain role in the pathology of productive animals, leading to a weakening of the body's immunobiological forces to various diseases and significantly reducing the productivity of animals.

Among the main widespread and dangerous helminthiasis in cattle, sheep, and goats “except for larval cestodiasis” are fascioliasis, anoplocephalatoses, in particular monieziosis and gastrointestinal strongylatoses.

Ascariasis, esophagostomosis, and trichocephalosis, and for birds (chickens) – ascariasis and heterakidosis are among the helminthiasis, which are widespread and pose a danger to pigs.

Horse helminthiasis, such as strongylosis, strongyloidiasis, trichonematosis, anoplocephalatoses, and in some regions, fascioliasis, oxyuriasis, etc., are quite widespread and dangerous.

The control of helminthiasis should be comprehensive and cover all the details of this complex, namely: planned therapeutic and prophylactic deworming, the volumes, timing and frequency of which should be based on the results of studying the regional epizootology of helminthiasis in each specific climatic and geographical zones; implementation and widespread use of methods and means of pasture prevention, including the neutralization of the external environment in relation to eggs and larvae of pathogens of geohelminthiasis, as well as control of the main, intermediate, and additional hosts for pathogens of biohelminthiasis; for some species of animals, for example, for sheep and goats, the use of methods and means of chemoprophylaxis, for example, feeding anthelmintic-salt mixtures; measures aimed at increasing the natural immunobiological resistance of the animal organism to various helminthiasis, through the use of biological stimulants – vitamin complexes, micro- and macroelements, immunostimulants.

References

- Akopian, V. D. (1960). Snizhenie "A"-vitaminnoj cennosti pecheni pri jeksperimental'nom fascioljoze i cistikauljoza ovec [Decrease in vitamin A value of the liver in experimental fascioliasis and cysticaulosis of sheep]. *Bulleten n-t inform. Armyansk. NIIZHIV*, 4-5, 57-60.
- Akopian, V. O. (1956). Vlijanie vitamina "A" na povyshenie rezistentnosti ovec k cistikauljozu [The effect of vitamin A on increasing the resistance of sheep to cysticaulosis]. *Trudy Arm.NIIZHIV*, 1(9), 126-136.
- Alavi, S. E., & Shahmabadi, H. E. (2021). Anthelmintics for drug repurposing: Opportunities and challenges. *Saudi Pharmaceutical Journal: SPJ*, 29(5), 434. doi: 10.1016/j.jsps.2021.04.004
- Amonov, O. Z. (2008). Novye antgel'mintno-solevye smesi protiv gel'mintozov v karakulevodskih hozjajstvah i tehnologija ih primenenija [New anthelmintic-salt mixtures against helminthiasis in karakul farms and the technology of their application]. (Abstract of dissertation of Candidate of Veterinary Sciences). Samarkand.
- Arias, M. S., Cazapal-Monteiro, C. F., Suárez, J., Miguélez, S., Francisco, I., Arroyo, F. L., ... & Mendoza de Gives, P. (2013). Mixed production of filamentous fungal spores for preventing soil-transmitted helminth zoonoses: a preliminary analysis. *BioMed research international*, 2013. doi: 10.1155/2013/567876
- Azimov, D. A. (1963). Gel'minty i gel'mintozy ovec juga Uzbekistan [Helminths and helminthoses of sheep in the south of Uzbekistan]. (Abstract of dissertation of Candidate of Veterinary Sciences). Moscow.
- Azimov, Sh. A. (1974). Fascioljozy i anoplocefaljozy ovec i krupnogo rogatogo skota v Uzbekistane [Fascioliasis and anoplocephalatoses of sheep and cattle in Uzbekistan]. Tashkent: FAN UzSSR.
- Badanin, N. V. (1949). Voprosy jepizootologii glavnejshih gel'mintozov karakul'skoj ovcy [Questions of epizootology of the main helminthiasis of the Karakul sheep]. *Trudy Uzbek Agricultural Institute*, 7, 3-21.
- Boev, S. N., & Redko, A. S. (1947). Opyt profilaktiki diktikauljoza i trihostrongilidozov ovec metodom vol'noj dachi soli s primes'ju fenotiazina [Experience in the prevention of dictyocaulosis and trichostrongylidosis in sheep by the method of free giving of salt with an admixture of phenothiazine]. *Veterinaria*, 3.
- Cabaret, J., Bouilhol, M., & Mage, C. (2002). Managing helminths of ruminants in organic farming. *Veterinary research*, 33(5), 625-640. doi: 10.1051/vetres:2002043
- Charlier, J., De Waele, V., Ducheyne, E., van der Voort, M., Velde, F. V., & Claerebout, E. (2015). Decision making on helminths in cattle: diagnostics, economics and human behaviour. *Irish Veterinary Journal*, 69(1), 1-5.
- Charlier, J., Rinaldi, L., Musella, V., Ploeger, H. W., Chartier, C., Vineer, H. R., ... & Claerebout, E. (2020). Initial assessment of the economic burden of major parasitic helminth infections to the ruminant livestock industry in Europe. *Preventive Veterinary Medicine*, 182, 105103. doi: 10.1016/j.prevetmed.2020.105103
- Daugalieva, E. Kh., & Oripov, A. O. (1990). Primenenie immunostimuljatorov dlja profilaktiki gel'mintozov i povyshenija rezistentnosti zhitovnyh (metodicheskie rekomendacii) [The use of immunostimulants for the prevention of helminthiasis and increasing the resistance of animals (guidelines)]. Moscow.
- Davtian, E. A., & Akopian, V. D. (1958). Izmenenie balansa vitamina "A" u ovec pri jeksperimental'nom fascioljoze Changes in the balance of vitamin A in sheep with experimental fascioliasis. *Izvestiya ANArmSSR, biological and agricultural sciences*, 11, 17-26.
- Demidov, N. V. (1982). *Antgel'mintiki v veterinarii* [Anthelmintics in veterinary medicine]. Moscow: Kolos.
- Demidov, N. V., & Potemkina, V. A. (1980). *Spravochnik terapii i profilaktike gel'mintozov zhitovnyh*. [Handbook of therapy and prevention of helminthiasis in animals]. Moscow: Kolos.
- Devleeschauwer, B., Ale, A., Torgerson, P., Praet, N., Maertens de Noordhout, C., Pandey, B. D., ... & Speybroeck, N. (2014). The burden of parasitic zoonoses in Nepal: a systematic review. *PLoS neglected tropical diseases*, 8(1), e2634. doi: 10.1371/journal.pntd.0002634
- Dolnikov, Yu. Ya. (1956). Group deworming of pigs with fluorosilicate on trium with ascariasis. *Veterinaria*, 5, 38-40.
- Dzhabborov, Sh. A. (2005). Development and implementation of new anthelmintic-salt mixtures against helminthiasis in sheep. (Abstract of dissertation of Candidate of Veterinary Sciences). Samarkand.
- Dzhabborov, Sh. A. (2017). The effectiveness of anthelmintic measures and ways to increase it. (Abstract of dissertation of Doctor of Veterinary Sciences). Samarkand.
- Foster, N., & Elsheikha, H. M. (2012). The immune response to parasitic helminths of veterinary importance and its potential manipulation for future vaccine control strategies. *Parasitology research*, 110(5), 1587-1599. doi: 10.1007/s00436-012-2832-y

- Gorokhov, V. V. (1970). Himicheskie i biologicheskie metody bor'by s mollyuskami – promezhutochnymi hozyaevami gel'mintov [Chemical and biological methods of control of snails – intermediate hosts of helminths]. Gel'mintozy sel'skohozyajstvennyh zhivotnyh. 1969. Itogi nauki VINITI, 132-170.
- Hewitson, J. P., & Maizels, R. M. (2014). Vaccination against helminth parasite infections. Expert review of vaccines, 13(4), 473-487. doi: 10.1586/14760584.2014.893195
- Idris, O. A., Wintola, O. A., & Afolayan, A. J. (2019). Helminthiasis; prevalence, transmission, host-parasite interactions, resistance to common synthetic drugs and treatment. Heliyon, 5(1), e01161. doi: 10.1016/j.heliyon.2019.e01161
- Irgashev, I. Kh. (1963). Gel'mintozy melkogo rogatogo skota v uslovijah Uzbekistana [Helminthiasis of small cattle in conditions of Uzbekistan]. (Abstract of dissertation of Doctor of Veterinary Sciences). Moscow.
- Irgashev, I. Kh. (1963)^a. Novoe v bor'be s vazhnejshimi gel'mintozami karakul'skih ovec v Uzbekistane [New in the fight against the most important helminthiasis of Karakul sheep in Uzbekistan]. Trudy VNIIC, 13.
- Irgashev, I. Kh. (1963)^b. Primenenie v karakulevodcheskih hoz'jajstvah fenotiazino-solevoj smesi s dobavleniem mednogo kuporosa i molibdena [Application in karakul farms of phenothiazine-salt mixture with the addition of copper sulfate and molybdenum], Proceedings of scientific conference, dedicated to the 90th anniversary of the Kazan veterinary institute. Kazan.
- Isaev, Zh. M. (2019). Osnovnye gel'mintozy loshadej (*Equus caballus*), loshadi przhival'skogo (*Equus przewalski*) i kulanov (*Equus hemionus*) [The main helminthiasis of horses (*Equus caballus*), horses of the przewalski (*Equus przewalski*) and kulans (*Equus hemionus*)]. (Abstract of dissertation of PhD in Veterinary Sciences). Samarkand.
- Kotze, A. C., Gilleard, J. S., Doyle, S. R., & Prichard, R. K. (2020). Challenges and opportunities for the adoption of molecular diagnostics for anthelmintic resistance. International Journal for Parasitology: Drugs and Drug Resistance, 14, 264-273. doi: 10.1016/j.ijpddr.2020.11.005
- Kuznetsov, M. I. (1972). Anoplocefal'jatozy zhvachnyh zhivotnyh [Anoplocephalatoses of ruminants]. Moscow: Kolos.
- MacDonald, A. S., Araujo, M. I., & Pearce, E. J. (2002). Immunology of parasitic helminth infections. Infection and immunity, 70(2), 427-433. doi: 10.1128/IAI.70.2.427-433.2002
- McSorley, H. J., & Maizels, R. M. (2012). Helminth infections and host immune regulation. Clinical microbiology reviews, 25(4), 585-608. doi: 10.1128/CMR.05040-11
- Mereminskii, I. A. (1967). Prognozirovanie fascioljoza i paramfistomatozov zhvachnyh zhivotnyh [Prediction of fascioliasis and paramphistomatosis in ruminants]. Veterinaria, 5, 76-78.
- Morgan, E. R., Charlier, J., Hendrickx, G., Biggeri, A., Catalan, D., Samson-Himmelstjerna, V., ... & Vercruyse, J. (2013). Global change and helminth infections in grazing ruminants in Europe: impacts, trends and sustainable solutions. Agriculture, 3(3), 484-502. doi: 10.3390/agriculture3030484
- Nepoklonov, Ya. D. (1959). K voprosam jepizootologii glavnejshih gel'mintozov ovec v Kashkadar'inskoj oblasti Uzbekskoj SSR [On the issues of epizootology of the main helminthiasis of sheep in the Kashkadarya region of the Uzbek SSR]. Bolezni selskohoziastvennyh zhyvotnykh. Sbornik nauchnyh trudov NIVI Uzbek, 13, 95-102.
- Nixon, S. A., Welz, C., Woods, D. J., Costa-Junior, L., Zamanian, M., & Martin, R. J. (2020). Where are all the anthelmintics? Challenges and opportunities on the path to new anthelmintics. International Journal for Parasitology: Drugs and Drug Resistance, 14, 8-16. doi: 10.1016/j.ijpddr.2020.07.001
- Noon, J. B., & Aroian, R. V. (2017). Recombinant subunit vaccines for soil-transmitted helminths. Parasitology, 144(14), 1845-1870. doi: 10.1017/S003118201700138X
- Oripov, A. O. (1978). Deworming of sheep against strongylatosis. Veterinariia, 4, 74.
- Oripov, A. O. (1978)^a. Degel'mintizacija ovec protiv strongil'jatozov lechebno-kormovymi granulami [Deworming of sheep against strongylatosis with medicinal feed granules]. Trudy UzNIVI, 27, 88.
- Oripov, A. O. (1980). Principy razrabotki i perspektivy metodov gruppovoj degel'mintizacii zhivotnyh [Principles of development and prospects of methods for group deworming of animals], Proceedings of the conference VOG USSR Academy of Sciences, 30, 78-82.
- Oripov, A. O. (1983). Trihostrongilidozy ovec v Uzbekistane [Trichostrongylidosis of sheep in Uzbekistan]. (Abstract of dissertation of Doctor of Veterinary Sciences). Moscow.
- Oripov, A. O. (1990). Degel'mintizacija ovec protiv strongil'jatozov [Deworming of animals with medicinal feed granules and medicinal feed mixture]. Trudy UzNIVI.
- Oripov, A. O., & Dzhabborov, Sh. A. (2000). Razrabotka novyh antgel'mintno-solevyh smesej protiv gel'mintozov ovec [Development of new anthelmintic-salt mixtures against helminthiasis in sheep].

- Ўzbekistonda qishloq khǎzhalik ǎaivonlar kasalliklariga qarshi kurash va oldini olish tadbirlari (Ilmiy maqollar toplami), Samarkand, 68-72.
- Oripov, A. O., & Dzhabborov, Sh. A. (2003). Novoe sredstvo dlja profilaktiki gel'mintozov ovec [A new remedy for the prevention of helminthiasis in sheep], Actual problems of animal diseases in modern conditions. proceedings of the International conference dedicated to the 60th anniversary of the Taj. NIVI, November 22, 2003. Dushanbe.
- Oripov, A. O., & Petrosian, A. S. (1974). Gruppovoj metod degel'mintizacii ovec nilvermom [Group method for deworming sheep with nilverm]. Veterinariia, 3, 64-65.
- Oripov, A. O., Dzhabborov, Sh. A., & Yuldashev, N. E. (2020). Novye metody i sredstva lecheniya i profilaktika gel'mintozov karakul'skih ovec [New methods and means of treatment and prevention of helminthiasis of Karakul sheep], Proceedings of the international scientific and practical conference "Prospects for the deepland livestock development" dedicated to the 90th anniversary of Education Research Institute of Karakul Breeding and desert ecology, Samarkand-December 10-11, 2020.
- Oripov, A. O., Khalikov, S. S., Isaev, Zh. M., & Ulashev, I. A. (2020). Effektivnost' mehanokompleksov nekotoryh antgel'mintikov protiv gel'mintozov ovec [The effectiveness of mechanocomplexes of some anthelmintics against helminthiasis in sheep], Proceedings of scientific conference in veterinary medicine and biotechnology. Samarkand.
- Oripov, A. O., Salimov, B. S., Dzhabbarov, Sh. A., & Yuldashev, N. E. (2020). Guidelines for treatment and prevention of helminthiasis in livestock. Tashkent.
- Oripov, A. O., Shokhidoyatov, Kh. M., Khidirova, N. K., Mamatkulova, N. M., Akhmedov, B. N., & Ulashev I. A. (2016). Stimulirujushhee dejstvie gossiprena na produktivnost' kur [Stimulating effect of gossiprene on the productivity of chickens], V International conference Distribution and control measures for especially dangerous diseases of animals and birds, August 25–26, 2016. Samarkand.
- Oripov, A. O., Yuldashev, N. E., Elmurodov, B. Zh., Nasrullaev, A. O., & Ulashev, I. A. (2016^a). Antgel'mintnaja aktivnost' 2-acetilaminobenzimidazola (2-ACB) i ego gidrohlordnogo soedinenija (2-ACB.HCl) [Anthelmintic activity of 2-acetylaminobenzimidazole (2-ACB) and its hydrochloride compound (2-ACB HCl)], V International conference Distribution and control measures for especially dangerous diseases of animals and birds, August 25–26, 2016. Samarkand.
- Oripov, A. O., Yuldashev, N. E., Elmurodov, B. Zh., Nasrullaev, A. O., & Ulashev, I. A. (2016^b). Fasciolocidnaja aktivnost' digidrohinozolin-4 [Fasciolocidal activity of dihydroquinosolin-4], V International conference Distribution and control measures for especially dangerous diseases of animals and birds, August 25–26, 2016. Samarkand.
- Reda, A. A. (2018). Probiotics for the control of helminth zoonosis. Journal of veterinary medicine, 2018, 4178986. doi: 10.1155/2018/4178986
- Rehman, A., & Abidi, S.M.A. (2021). Livestock health: current status of helminth infections and their control for sustainable development, In R. C. Sobti (Ed.), Advances in Animal Experimentation and Modeling (pp. 365–378), United Kingdom: Academic Press. doi: 10.1016/B978-0-323-90583-1.00029-5.
- Robinson, M. W., & Dalton, J. P. (2009). Zoonotic helminth infections with particular emphasis on fasciolosis and other trematodiasis. Philosophical Transactions of the Royal Society B: Biological Sciences, 364(1530), 2763-2776. doi: 10.1098/rstb.2009.0089
- Sadykov, V. M. (1973). Jehinokkoz i bor'ba s nim [Echinococcosis and the fight against it]. Moscow.
- Salimov, B. S. (1974). Jeksperimental'nye issledovanija po dikrocelioz zhivotnyh, jepizootologija zabolevanija i mery bor'by s nim v Uzbekistane [Experimental studies on animal dicroceliosis, epizootology of the disease and measures to combat it in Uzbekistan]. (Abstract of dissertation of Doctor of Veterinary Sciences). Moscow.
- Tinkler, S. H. (2020). Preventive chemotherapy and anthelmintic resistance of soil-transmitted helminths—Can we learn nothing from veterinary medicine? One Health, 9, 100106. doi: 10.1016/j.onehlt.2019.100106
- Tsotetsi, A. M., Njiro, S., Katsande, T. C., Moyo, G., & Mpofu, J. (2013). Prevalence of gastrointestinal helminths and anthelmintic resistance on small-scale farms in Gauteng Province, South Africa. Tropical animal health and production, 45(3), 751-761. doi: 10.1007/s11250-012-0285-z
- Waller, P. J. (2006). From discovery to development: current industry perspectives for the development of novel methods of helminth control in livestock. Veterinary parasitology, 139(1-3), 1-14. doi: 10.1016/j.vetpar.2006.02.036
- Yuldashev, N. (2020). Anthelmintic-salt mixtures – an effective means in prevention of helminthiasis in sheep. Ukrainian Journal of Veterinary Sciences, 11(4), 4-12. doi: 10.31548/ujvs2020.04.001

- Yuldashev, N. (2020). New molluscicides in control of freshwater snails – intermediate hosts for causative agents of fascioliasis, paramphistomatosis and orientobilharziasis. Scientific reports of NULES of Ukraine, 0(6(88)). doi: 10.31548/dopovidi2020.06.022
- Yuldashev, N. E. (2018). Sovremennye metody i sredstva bor'by s gel'mintozami [Modern methods and means of the control of helminthiasis]. (Abstract of dissertation of Doctor of Veterinary Sciences). Samarkand.
- Yuldashev, N. E., & Oripov, A. O. (2016). Poisk novyh molljuskocidov protiv presnovodnyh molljuskov [Search for new molluscicides against freshwater snails], V International conference Distribution and control measures for especially dangerous diseases of animals and birds, August 25–26, 2016. Samarkand.
- Zharikov, I. S. (1975). Profilaktiki gel'mintozov krupnogo rogatogo skota v promyshlennyh zhivotnovodcheskih kompleksah Belorusskoj SSR [Prevention of helminthiasis in cattle in industrial livestock complexes of the Byelorussian SSR]. Problemy komplektovanija ferm zhivotnymi i veterinarnaja ohrana, 190-196.

СУЧАСНА СТРАТЕГІЯ, НОВІ МЕТОДИ І ЗАСОБИ БОРОТЬБИ З ГЕЛЬМІНТОЗАМИ В УЗБЕКІСТАНІ

А. О. Оріпов, Н. Е. Юлдашев

***Анотація.** Сучасна стратегія боротьби проти основних, широко розповсюджених гельмінтозів сільськогосподарських тварин передбачає проведення комплексу протигельмінтозних заходів, що включає: планові лікувально-профілактичні дегельмінтизації, які ґрунтуються на даних вивчення епізоотології гельмінтозів у кожній конкретній клімато-географічній зоні; здійснення заходів пасовищної профілактики геогельмінтозів і боротьбу з основними, проміжними й додатковими господарями збудників біогельмінтозів, у тому числі й зоонозних гельмінтозів (ехінококозу, ценурозу й цистицеркозів); здійсненні заходів хіміопротифілактики гельмінтозів у деяких галузях тваринництва, наприклад, у вівчарстві; за допомогою застосування антигельмінтно-сольових сумішей; використання коштів, що підвищують імунобіологічні захисні властивості організму тварин до гельмінтозів та інших захворювань за допомогою широкого застосування вітамінів, мікро- та макроелементів та інших біологічних стимуляторів.*

***Ключові слова:** гельмінти, гельмінтози, дегельмінтизація, моллюскоциди, антигельмінтики, антигельмінтно-сольові суміші, імностимулятори*

*Economics is a difficult discipline and requires special knowledge,
but no one will ever believe it
John Keynes*

UDC 330: 636/.09

INTRODUCTION TO THE ECONOMICS OF ANIMAL HEALTH IN UKRAINE

ZHUKOVSKY M.O., assistant

OrcID: 0000-0002-6158-800X

NEDOSEKOV V.V., Doctor of Veterinary Sciences, Professor,

OrcID: 0000-0001-7581-7478

National University of Life and Environmental Sciences of Ukraine, Kyiv, Ukraine

Email: nfvm@ukr.net

Abstract. *The world has long recognized the importance of studying the economic impact of animal health problems on the livestock, the veterinary service and the economic and food safety of the country as a whole. Animal health economics is a branch of the economy and, in particular, the agricultural economy, which applies the principles and methods of economic analysis to animal health problems. It is established that it has already been quite successfully integrated into the veterinary services of developed countries and in the curricula of the leading faculties of veterinary medicine.*

The article examines the foundation, stages of formation and development of the animal health economy. The main scientific schools and their contribution to the development of animal health economics are highlighted.

In Ukraine so far the scale of the animal health economy has been quite modest. The concept was based on disease losses and a cost-benefit analysis of disease control or coping strategies. It is extremely necessary to establish its own scientific school that will take into account the world experience, realities and features of veterinary medicine and animal husbandry and be implemented in modern science and production of Ukraine.

In our opinion, the animal health economy in Ukraine should include the following components: economic theory and methods, health economics, economic analysis of diseases, economics of veterinary business.

Knowledge of the basics of animal health economics allows the veterinarian to more effectively cover all areas of work from the state veterinary inspector to the doctor at the farm level, to be a real consultant on effective animal husbandry. This knowledge also adds value to private practitioners, making them better prepared to compete in the veterinary services market. Animal health economics should be included in the training program for veterinarians in Ukraine.

Key words: *animal health economics, economic analysis, control infection diseases, anti-epizootic measures, animal husbandry, economic efficiency of veterinary measures*

Introduction. The economy is an integral part of our lives. Regardless of our interest in the economy, the economy always affects our lives - what we do, in what conditions we live, what and how we eat, how we rest, how we develop and receive education, how we treat ourselves and treat our animals. Every day we have to take a lot economic decisions: to ensure their well-being, to cooperate with staff, suppliers, representatives of state institutions, to make economic decisions that will be have an impact on us in the long run.

Almost two-thirds of the population in Ukraine now live in urban conditions, where they have the best access to work, a higher standard of living, a better developed social sphere and simplified access to benefits of civilization, but limited or no access to land, livestock and food production. It implies the dependence of most people on agricultural producers. Ago, the effective functioning of this sector of the economy, in particular, the livestock sector, which covers all aspects: production, supply, processing, logistics and sales, has become a critical issue for guaranteeing the country's food security.

In the context of globalization, it is important to gain knowledge at the intersection of different specialities and it becomes important to provide economic justification for any veterinary activities to improve and protect animal health through funding and organization of activities. How both private business and the public sector operate within the current legislation and use to assess the effectiveness of well-known economic instruments. However, Theoretical principles and economic tools that shed light on the problems are currently little-studied animal health and the functioning of the veterinary service. At the production level, economic

theory and tools are especially important when planning veterinary activities, distributing financial resources, the effectiveness of anti-epizootic work and ensuring the appropriate level veterinary service.

Analysis of recent researches and publications.

Animal health economics in a very short time of its formation and development has already been integrated into the training programs of students of leading faculties of veterinary medicine. However, a small group of scientists, consultants and specialists is currently working on this area of research. Among them are: Bennet R. M., Buhr B. L., Carpenter T. E., Chilonda P., Davidson J. N., Dijkhuizen, A.A., Ellis, P.R., Hugh-Jones, M.E., Hurd H.S., Kaneene J.B., McInerney, J.P., Mlangwa J.E.D., Morris, R.S., Ngategize P.K., Otte M.J., Perry, B.D., Renkema J.A., Rushton, J., Stott, A.W., Tisdell C., Vagsholm I. and others.

Purpose. The purpose of the study is to investigate the beginnings, stages of formation and development of the economy animal health. Identify the main scientific schools and their contribution to the development of animal health economics. Define and thoroughly structure the components of animal health economics. Consider each of the components and identify features. Assess the state of economic research from this direction in Ukraine.

Materials and methods of research. Research materials were: data from literature sources, statistical information, FAO data. Statistical, analytical, historical, system methods, as well as system-activity approach are used.

Results of the research and their discussion.

The importance of farm animals in the modern world is difficult to exaggerate. First of all, it is food security of people, products of animal origin are contained in a third of products presented on store shelves. Raw materials of animal origin are used in light, food, cosmetics and pharmaceutical industries. Farm animals are the main part of mammals in the world and is an important part of aquatic biomass. In addition, billions of Pets around the world are serious capital, investment and working capital. Only in Ukraine according to the State Statistics Committee (2020) in the field of agriculture, forestry and fishing almost three million people are officially employed on the farm. This is more than in the industry, construction, education. And yet, the private sector and own households are not taken into account. The world of agriculture employs more than 700 million people. This is a colossal labour market where quantity employees are independent of fashion, political decisions, international conflicts and other factors macroenvironment, and most importantly it is a significant part of the world economy. Livestock is the most labour-intensive branch of agriculture. Also, unlike the crop industry provides work and income all year round, not seasonal. That is why, ensuring the health and welfare of animals, and accordingly, the food security of countries is one of the important tasks of the world community. These tasks must be considered in the political, social and economic context.

To make an economic assessment of health and veterinary animal care, it is important to have an understanding of the socio-economic conditions in which it operates a branch of animal husbandry and veterinary care of animals is carried out. Often found animal diseases, the origin and spread of which are closely related to socio-economic human activities. International, national policy, subsidies, product market regulation animal husbandry, the epizootic situation in the country and the world, the development of the pharmaceutical market and many other factors have both direct and indirect effects on the economy of animal health. Animal health economics is quite a young direction compared to other economic disciplines. And the first scientific schools in this area of research appeared only in the 1960s.

Peter Ellis (1972) and Heinz Konigshofer (1977) in the mid-1960s documented the information received from the veterinary services of different countries and concluded the so-called "Health Yearbook", which made a thorough assessment of the economic losses for each infectious disease, which are the most common. Peter Ellis was a lot in

why a pioneer in animal health economics, he is the founder of the Department of Epidemiology and Economics Animal Health (VEERU) at the University of Reading UK. The Efforts of Peter Ellis in economic development, animal health was assessed by the EU Economic Council and established in 1975 Department of Epidemiology and Animal Health Economics VEERU.

Tim Carpenter (1979, 1980) was another pioneer in health economics animals during the 1970s. His early work was on the economics of *Mycoplasma gallisepticum* and

Mycoplasma meleagridis in turkeys. Carpenter was the first to study the use of various methods of economic analysis of the study of diseases and their control. These are methods such as microeconomic disease analysis, simulation models for animal disease assessment, dynamic programming, assessment surplus consumers, willingness to pay for vaccinations, linear programming, use economic analysis to review subsidies to veterinary institutions and others.

Martin Hugh-Jones (1975), worked in the Department of Epidemiology and Health The University of Louisiana specializes in geographic information systems (GIS), modelling diseases such as anthrax, anaplastic

dermatophilosis and trypanosomiasis. He is famous for careful assessment of the economic impact on production by infectious diseases.

John McInerney (1996) and Keith Howe (Keith Howe, 1992), worked at the University of Exeter, UK. They began research on the theoretical foundations of animal health economics and conceptual model of farmers' behaviour during epizootics. Scientists tried to teach their fellow veterinarians new approaches to disease assessment. However, their views on the economics of animal health were largely limited to concepts and theories. This group is considered the first to initiate the conceptual foundations of economic analysis of the disease and its control.

Alt Dijkhuizen (1995) (Wageningen, The Netherlands) began in the 1970s study of the economic costs of the disease with an emphasis on mastitis. He also studied economics surgery in animal husbandry and production problems. In 1997, together with Roger Morris, (1997) published a textbook on animal health economics which described in detail such issues as basics economic analysis of animal diseases, decision-making in animal health management, economic consequences of outbreaks of infectious animal diseases, linear programming in economic analysis herd health, dynamic programming to optimize the treatment of animal diseases, risk management in the elimination of disease outbreaks and more.

Tisdell, Harrison and Ramsay (1995) began to study economics animal health in the second half of the 1990s at the Universities of Queensland and Brisbane, Australia. We started with a study of the economics of cattle health, with an emphasis on foot and mouth disease. Analysed the cost of elimination of foot-and-mouth disease and the economic effect of eliminating this disease.

Brian Perry (2001) - ILRI Institute in Nairobi (Kenya) - is one of the most famous epidemiologists from 1990 to the 2000s. He brought together several important topics in animal health economics: economic analysis and forecasting at the farm level; the impact of sanitary requirements on profitability and market of livestock products and financing of veterinary services at the state level. In addition, Perry, with Tom Randolph (2001) and John McDermott (2002) quite fruitfully cooperated in the field of economics of parasitic animal diseases and discovered the relationship between poverty and virtually no investment in animal health in countries Of the African continent.

Richard Bennett (2003) from the University of Reading UK also made his contribution to the study of animal health economics, he initially worked on the economic foundation's control of cattle leptospirosis. But his main contribution to this day is his research work on animal welfare economics and the assessment of endemic disease losses in the UK.

Jonathan Rushton (2016) is an economist specializing in health economics animals, the economics of animal husbandry and the development of this industry. He has experience in livestock development in Africa, Asia, Europe and Latin America works with many governmental and non-governmental organizations. He currently teaches animal health economics at the Royal Veterinary College, London. He investigates food security, reducing production costs animal husbandry, animal welfare, optimization of veterinary costs for prevention and localization of transboundary emergent animal diseases in developing countries and more. The author of the textbook of animal health economics and animal husbandry economics.

Joachim Otte (2007), his research is funded by FAO. Uses different economic approaches and methods are aimed at making decisions to ensure animal health in industrial livestock. Issues of animal health economics and anti-epizootic funding measures in close connection with political, social and economic aspects.

Alistair Stott (2005) is a representative of a Scottish agriculture college. He first applied the method of optimization and feasibility in decision-making treatment and prevention of animal diseases, in 2005 his monograph was published. During the Soviet era, research was also conducted to determine the economic damage caused by animal diseases and the cost-effectiveness of veterinary measures. During the times of independent Ukraine, no new research has been conducted in the field of animal health economics. From the above, we can draw an intermediate conclusion that the economics of animal health has already been integrated into veterinary services around the world and doctors' training programs in veterinary medicine in universities.

Economics includes economic theory and the methods used for analysis economic problems or for planning for the future. In order to apply effectively economic laws and principles of management in agriculture, the economist must understand biological principles of agricultural production. And when it comes to health economics animals, the basics of animal husbandry and the principles of veterinary medicine. In our opinion, the animal health economy is a branch of the economy and, in particular, the economy agriculture, which applies the principles and methods of economic analysis to health problems animals. Quite often the economy is defined as an industry that measures things in monetary terms, in that time when other disciplines use physical units: number of animals, live weight gain, body temperature, milking and more. This view is fundamentally wrong and even demeans this field of knowledge. The economy is not about money. Economics

helps to make rational decisions in distribution limited resources, using different methods of economic analysis.

Currencies serve as criteria for comparing different resources and achieving goals as well, take direct participation in decision-making. Livestock economics and animal health help to decide problems of lack of resources. Decisions concerning the allocation of limited resources by owners of animals, agribusiness, veterinary specialists, government officials, should be balanced and well analysed with the help of various economic instruments. Decision which will bring the greatest benefit in terms of resources used will be rational.

According to John McNerney (1987), the underlying conceptual models Economic analysis includes three main components: people, product and resources. People want a certain product and make decisions, products are goods and services that satisfy human needs, and resources are the basis for product production and resources are the starting point economic activity.

Animal diseases have a negative impact on the process of transforming resources or factors production into a product, goods and services available to people. Animal diseases lead to direct economic losses for the producer and the potential loss of product value for the consumer. Ago animal diseases have a significant impact on the regional, national and global economy as a whole. The analysis of such systemic influence is complex and multi-vector.

Animal health is not a problem, disease is a problem. A world with perfect competition would be ideal, where all manufacturers had equal access to the latest technology, access to all required resources in unlimited quantities, minimum production costs, and total people's well-being was constantly growing. But alas, we all understand that to achieve such a balance in economy is unrealistic. The same situation with animal diseases. Imagine a world where no animal is sick, does not become infected, does not die is not possible. But we can and in most cases take action preventing the spread of infectious diseases, reducing morbidity, preventing death animals, minimizing the period of reduced productivity, etc. This becomes more important in quality assistance in deciding on animal health measures at various levels.

In our country, the scale of the animal health economy was quite modest. The concept was based on losses (losses) due to disease and cost-benefit analysis of control strategies or overcoming diseases. This work can be called economic analysis of animal diseases and strategies liquidation conditionally. In the past, economic principles and methods for analysis have been little used veterinary systems, management of such systems, analysis of animal health policy, impact development of veterinary business on animal health and much more. This situation has changed in the world a few decades ago with the contribution of livestock experts, political scientists, economists and veterinarians who are interested in the management of veterinary systems.

The development of the animal health economy has had a positive impact on:

- financing of veterinary services in different countries;
- quality of veterinary services;
- division of responsibilities between the state and private practitioners;
- planning and level of financing of anti-epizootic measures.

In our opinion, the animal health economy in Ukraine should include the following components:

- economic theory and methods;
- health economics;
- economic analysis of diseases;
- economics of veterinary business (Fig. 1).

Economics is the object of knowledge of many sciences, each of which chooses its subject for analysis and research, ie the range of phenomena, processes and laws that are characterized by specific features and combined into a certain system of knowledge. Economic theory in the system of economic sciences occupies a central place. Economic theory is a set of interrelated scientific categories, laws, propositions and hypotheses. These hypotheses take the form of models of economic behavior, and each model can be tested empirically. Economic models are abstract logical constructions consisting of two components: assumptions and the consequences of such assumptions (Parkin M., King D. 1992). The theory can be used to describe, explain, or predict the economic behavior of subjects or economic variables. In addition, it is the theory that directs the direction of research. Thus, economic theory guides economists in choosing appropriate concepts, models, methods and techniques for the study of economic problems and data analysis in both basic and applied work.

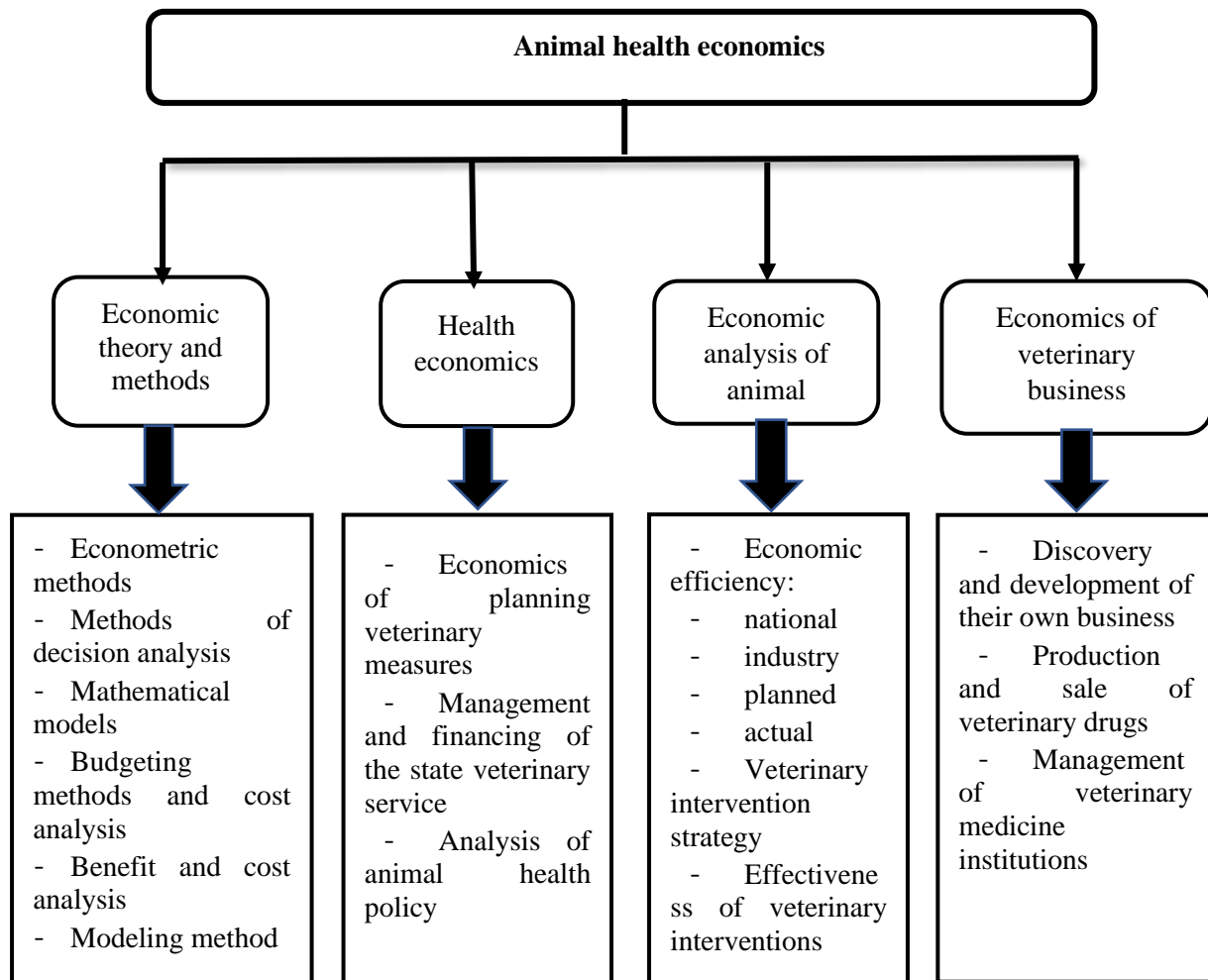


Figure 1. Components of animal health economics

What is the subject of science, such is its method of research: the subject generates the features of the method, and the method produces the tools of cognition, through which economists penetrate into the essence of economic phenomena and processes. Many of the methods are borrowed from related sciences: mathematics, mathematical statistics, accounting, psychology, management, biology, veterinary medicine and others, which are the result of the interpenetration of different sciences at certain stages of their development and feature of economic analysis, formed and developing at their intersection. In the scientific literature there is no unity on the classification of methods of economic analysis. The most appropriate is the classification of methods of economic analysis according to their internal content and purpose. In economic theory, the system method is widely used in analysis. It involves the consideration of each economic phenomenon as a system. Integrity is an important element of a systems approach that requires the study of individual components of any phenomenon and the study of internal relationships between these elements and subsystems, as well as identifying the overall purpose of the system. The researcher must establish the nature, place and role of each element of the system, their relationship. The synergetic approach to economic analysis is to consider the object of analysis as a complex system that is self-developing, the study of processes of self-organization, streamlining and maintaining the sustainability of the entity. The synergetic approach is the development of a systems approach, which traditionally studies the processes of maintaining balance in systems through feedback, as well as systems management processes.

Economic and mathematical methods are the conditional name of the methods of mathematics and cybernetics used to solve specific management problems. These include methods of multidimensional complex estimation, econometric, methods of mathematical programming (linear, nonlinear, dynamic, discrete) and others.

Factor analysis methods are used to study causal relationships or the influence of factors on performance. These include the following methods: deterministic (economic) factor analysis (chain substitutions, absolute

and relative differences, integral, partial participation, etc.). However, in the economy of animal health, as a rule, uses a relatively narrow range methods.

Morris argues that economic analysis of animal health problems uses five common methods of economic analysis (Morris, R.S. 1999). It:

- partial or full budgeting,
- profitability analysis,
- cost-benefit analysis,
- decision analysis
- system modeling.

Econometric methods (econometric modeling) are often used in animal health economics to predict production and socio-economic indicators or to study different approaches to disease prevention or control. The methods of models have a special place in determining the directions and assessing the prospects for the development of the field of research. The process of applying modeling methods is an important way of theoretical and practical actions aimed at stabilizing and ensuring the effective development of veterinary services. Statistical and epizootic models use Ngategize and Kaneene (Ngategize P.K. & Kaneene J.B., 1985). And Hurd examines in detail the application of "simulation" models (Hurd H.S., 1993). Buhr, Carpenter, Vagsholm pointed to the benefits of econometric methods for comparison and relationship in epizootology and economics (Buhr B. L., 1993, Carpenter T. E. 1991, Vagsholm I., 1991). The use of econometric methods of quantitative modeling in decision-making on the prevention, treatment and control of animal diseases was considered by Bennet R. M. (1992), Dijkhuizen A.A. (1991), Renkema J.A. (1980).

Decision analysis methods are used to make decisions in conditions of uncertainty, features in terms of warehousing, but poorly structured economic problems (Mlangwa J.E.D. and Samui K.L. 1996). Risk analysis is included in this methodology, which is based on the synthesis of expert opinion. Data on risk opportunities (empirical or variable) is significant. The equipment can be used at the manufacturer's level or at higher levels up to the international level. The models used in the methods of decision analysis can be divided into the following:

- mathematical
- technological schemes
- repayment matrices
- decision trees.

Davidson and co-authors gave an example of such an approach to thromboembolic meningoencephalitis in cattle (Davidson J. N. 1981).

Optimization of mathematical models uses linear programming. Although this technique is purely mathematical, it is a very useful tool in the allocation of resources and funding of anti-epizootic measures on a limited budget. The pioneers in this were: Bennet, Dijkhuizen, Ngategize (Bennet R. M. 1992, Dijkhuizen A.A. 1991, Ngategize P.K. 1985).

Budgeting methods and cost analysis in animal health economics are in fact the basis for planning anti-epizootic measures and calculating the effectiveness or feasibility of financing animal disease prevention. These methods are used by the vast majority of scientists in the field of animal health economics, public veterinary services of different countries and non-governmental organizations in the formation of annual or short-term plans. Budgeting methods are the basis of planning in the economics of animal health. They allow either to completely prevent the occurrence of diseases, or to minimize losses in diseases (to achieve the minimum cost of the disease). Moreover, it is effective both at the level of a small farm or agricultural enterprise, and at the level of an entire industry or country. Partial budgeting methods use the partial analysis methodology accordingly.

Benefit-cost analysis is used in cases where the planning of veterinary measures covers a period of more than one year. It can also be used in combination with a partial analysis methodology. This method is more often used at the national and international levels, in the implementation of multi-year programs for the rehabilitation of large areas, countries, regions and the development of programs to support and finance the fight against epizootics in poor countries. Socio-economic indicators are also taken into account in this method and the analysis of the corresponding level is carried out. The main purpose of this method of economic analysis is to achieve the desired result at minimal cost.

The last of the most widely used methods of economic analysis, but not the last in its importance is the method of modeling. It tries to simulate real variables (state, distribution, magnitude, quantity) over time. Typically, this method allows you to make decisions or analyze the relationship between the epizootic and economic model. Epizootic modeling is used in two ways. The first option is when individual animals in the herd are "supervised" for a certain period of time. Their state changes stochastically, i.e. in accordance with

the laws of probability. Alternatively, the livestock moves over time and these animals change their state deterministically using fixed transition factors (Bennet R. M. 1992, Mlangwa J.E.D. 1996). In stochastic modeling, the risk is taken into account by means of probability distribution or by means of random numbers. Simulation is a non-optimized method that is useful for analyzing the dynamics of variables in different scenarios. Economic variables can also be modeled.

Many methods and techniques have been used to analyze losses in disease control. The idea of choice is central to any economic analysis. The main premise of the analysis is to compare one disease control strategy with the consequences of inaction.

Economic analysis is not a form of financial accounting. The main task in the economics of animal health is to compare and create a rating of alternative disease control measures according to the preferences of each. Accordingly, make the most appropriate decision, rather than calculating the exact monetary value.

The economics also investigates the risks of investing in the control and prevention of animal diseases, and risk assessment is an important component of the animal health economics (Anteneha. 1991).

Control of animal diseases also involves the allocation of financial resources, both to prevent and further to combat diseases and their consequences (elimination of epizootic outbreaks, costs of treatment or destruction of animals, compensation to animal owners, etc.). All this together has a significant impact not only on the economy of farms, agricultural enterprises, large producers, but has a much broader impact. Including the competitiveness of the livestock industry and the economy as a whole. Because the crises in the livestock sector entail the processing industry, feed production, crop production, industry, exports, regional economies and, consequently, the national economy. That is why the economy of animal health is of the greatest importance for food and economic security of the country and, unlike economic theory, evolves much faster in its development. It also has significant differences depending on the country and continent, as well as crucial practical significance.

The most important factor in the animal health economy is the level of funding and the level of implementation of anti-epizootic measures. Three components are needed for full-fledged anti-epizootic measures in Ukraine - highly qualified veterinary specialists, legal framework and adequate funding. It should be noted that in recent years the underfunding of anti-epizootic measures has been systematic, which has prevented the competent authority from carrying out its functions under the anti-epizootic action plan, and as a result we have a tense epizootic situation in the country for some diseases. 2016 was a critical year, with funding amounting to only UAH 52.86 million. For comparison: a small country like Northern Macedonia in 2016 spent 4 million euros just to fight nodular dermatitis.

While in Ukraine in 2018 UAH 687.195 million was allocated for the implementation of the plan of anti-epizootic measures for the prevention of major infectious and parasitic animal diseases, in the future this amount remains stable, although at least the inflation index must be taken into account.

According to world practice and reports of competent authorities of different countries, to ensure the effective functioning of such a component of animal health economics as animal health economics, the ratio of budget expenditures for anti-epizootic measures to the cost of livestock products at market prices should be at least 0, 7-2%. Unfortunately, in Ukraine this figure does not exceed 0.06%.

In addition, unfortunately, in Ukraine there is only one source of funding for anti-epizootic measures - the state budget and the reserve fund at the national or regional level. This can be partly explained by the almost complete lack of attention from economists and research of the economic component of protection against the introduction and spread of infectious diseases in Ukraine.

While in many countries several sources are used. For example, in Germany and the Netherlands, there are several sources of funding for anti-epizootic measures and compensation for epizootics:

1. financing from the budget of the European Union;
2. financing at the expense of the state budget;
3. mutual funds of public-private financing are legally enshrined;
4. compulsory insurance funds;
5. voluntary insurance funds;
6. schemes that are not enshrined in law;
7. various voluntary funds.

It is clear that funding from the EU and the state budget will be present in any case, but almost all pet owners use public-private funding. Currently, in Germany and the Netherlands, anti-epizootic cash registers have been established in all lands, the legal mechanism of which is prescribed in the Animal Health Act.

Rat-Aspert and O. Krebs. also point out the effectiveness of systematic collective work in the field of combating infectious animal diseases. (Rat-Aspert. O., Krebs. S., 2011). Animal owners need to collectively manage this risk in order to improve their own welfare and ensure a high level of profitability in the livestock

industry. Manufacturers can collectively influence the level of anti-epizootic work. Their goal consists of two achievements: epizootic (elimination of the disease and restriction of the circulation of the pathogen) and economic (maximization of collective welfare).

The success of collective action depends on their acceptance by all producers and systematic work.

Economic analysis of animal diseases primarily includes the economic efficiency of veterinary measures. They are the prevented amount of losses in animal husbandry, the added value (obtained by increasing the number of products, improving its quality, savings labor and material resources due to the use of more effective means) and methods of disease prevention and treatment of animals, as well as savings in related industries.

In modern conditions, there are planned, actual, sectoral and national economic efficiency.

Planned economic efficiency is determined by substantiation of plans for prevention of infectious and non-communicable diseases, means and methods of treatment of animals, etc.

The actual economic efficiency is calculated based on the consequences of a set of preventive, health and therapeutic measures, the use of certain methods of treatment, tools and equipment.

Sectoral economic efficiency is calculated based on the consequences of veterinary measures, in particular, preventive, anti-epizootic, rehabilitation in a particular area of animal husbandry.

National economic efficiency is calculated as a result of veterinary measures that have been carried out in the livestock sector in the country as a whole and have had an impact on other related industries: processing, food, international trade and others.

The economic efficiency of veterinary measures can be calculated for the method of treatment or prevention, one animal, group of animals, farm, agricultural enterprise, livestock complex, settlement, district, region, region, industry, country.

Indicators of economic efficiency of veterinary measures are:

1. Reducing the incidence and mortality of animals;
2. Reduction of damages and losses;
3. Increasing the productivity of animals;
4. Increasing the number of livestock products;
5. Reduction of feed costs per unit of output;
6. Reducing the unit cost of production;
7. Increase profitability and increase profits.

In addition, economic analysis of animal diseases allows determining the profitability of specific programs for disease control and animal health management. Through economic analysis, quantitative assessment of the economic consequences of animal diseases, it is possible to develop approaches to optimize decisions on veterinary measures in the future and thus manage animal health (Ababneh, M., 2003).

The impact of animal diseases in the production system (livestock at different levels) is to reduce profitability and production results. The consequences of the disease can be divided into two groups: direct and indirect losses (losses) (Otte M.J., Chilonda P., 2013). Direct losses include:

- diseases destroy the main resource of animal husbandry, lead to the death of animals or cause their mass destruction;
- diseases reduce the efficiency and productivity of production processes, as an example of reduced feed absorption;
- Diseases reduce the productivity of animals, namely reduced milk yield, egg production, live weight gain, and most importantly, reduced quality and cost of production.

Indirect losses include the following:

- veterinary costs for the prevention, eradication or treatment of animal diseases (vaccination, veterinary drugs, quarantine costs, etc.);
- damage to human health due to zoonoses or consumption of low-quality contaminated products;
- suboptimal use of available resources by making forced changes in production (closing of export markets due to epizootic distress, other).

The economics of the veterinary business is a very significant area of the animal health economy. Starting your own business, licensing, working in market conditions. All these are civilized components of the market of veterinary services. If veterinary control and supervision is a function exclusively of the State Food and Consumer Service, then other aspects of veterinary activities (diagnosis, prevention, treatment, some anti-epizootic measures, production, sale of veterinary drugs and services, consultations, advisory activities, etc.) are a wide space for private veterinary business.

In countries where market relations have been developing for centuries (for example in developed European countries), about 80% of all veterinarians are involved in private practice. Forming your own private

veterinary practice cannot be an easy path. Therefore, everyone who dares to start their own business must find answers to many questions, master the basics of economic, financial and tax literacy, develop new skills. To be not only a doctor, but a good analyst, consultant, manager, to have the basics of foreseeing, to be interested in the socio-economic situation, and to monitor the epizootic situation both in the country and in the world.

Veterinarians, who understand the assessment of profits, profitability, production costs, compromise decisions in the elimination and treatment of diseases that can manage animal health will have more opportunities and demand among animal owners.

The practice of market relations proves that the market of veterinary goods and medicines is largely differentiated depending on consumer groups and consumer properties of veterinary goods. And this requires maximum consideration of the characteristics of its individual areas.

Conclusions and future perspectives. Animal health economics is an integrated dynamic field of production and research, which has already been integrated into veterinary services around the world and training programs for veterinarians in universities. In order to effectively apply economic laws and management principles in agriculture, it is necessary to comprehend the biological basis of animal husbandry and the principles of agricultural production. At the same time, animal health economics is based on animal health and the principles of veterinary medicine.

Of course, various groups of scientists, consultants and specialists are concerned with the issues of animal husbandry efficiency and animal health management. Currently, new priority areas for the development of animal health economics are the study of the economics of animal husbandry systems and animal health problems due to the impact of these systems, in particular transboundary emergent animal diseases. The feature of this economy direction is the priority of the implementation of laws and approaches of the "old economy" to the "new realities" - cross-border animal diseases and their impact and control.

Since Ukraine has for many years stood aside from the development of such areas of economic research as animal health economics and relied on the outdated system of determining the economic efficiency of veterinary measures, which inherited from the planned economy, it is now essential to start its own scientific school. This organization will take into account the world experience, realities, and features of the field of veterinary medicine and animal husbandry of our country.

Knowledge of the basics of animal health economics allows the veterinarian to more effectively cover all areas of work from the state veterinary inspector to the doctor at the farm level, helps to be a real consultant on effective animal husbandry. This knowledge also adds value to private practitioners, making them better prepared to compete in the veterinary services market.

Animal health economics should be included in the university curriculum for veterinarians in Ukraine to give students a sufficient understanding of economic concepts and tools and to prepare them for different roles and activities in their future careers.

References

Ababneh, M. (2003): Surveillance, Diagnosis and Control of 470 Brucellosis. Economic impact of small ruminant brucellosis; the regional Training Workshop: Amana, Jordan. Pp. 67-70.

Anteneha. (1991): The financing and staffing of livestock services in sub-Saharan Africa, across country analysis. Working Document No. 16. International Livestock.

Belaynew Alene, Mengistie Abebaw, Ayalew Negash (2016). A Review on Importance of Animal Health Economics in Decision Making. - Journal of Natural Sciences Research www.iiste.org ISSN 2224-3186 (Paper) ISSN 2225-0921 (Online) Vol.6, No.13, 2016

Ben Huntington, Theresa M., Bernardo, Mieghan Bruce (2021). Global Burden of Animal Diseases: a novel approach to understanding and managing disease in livestock and aquaculture. - Rev. Sci. Tech. Off. Int. Epiz., 2021, 40 (2)

Bennet R. M. (1992). - The use of 'economic' quantitative modelling techniques in livestock health and disease - control decision making: a review. Prev. vet. Med., 13 (1), 63-76.

Bennett, R.M. (1992) The use of economic quantitative modelling techniques in livestock health and disease-control decision making: a review. Preventive Veterinary Medicine 13, 63-76.

Bennett, R.M. (2003) The direct costs of livestock disease: the development of a system of models for the analysis of 30 endemic livestock diseases in Great Britain. Journal of Agricultural Economics 54, 55-72.

Buhr B. L. , Walker K . D . , Kliebenstein J . B . & Johnson S . R . (1993). - An industry level economic conceptual model of the effects of improved animal health. Prev. vet. Med., 16 (1), 3-14.

Carpenter T. E. (1991). - Veterinary economics - tips, tricks and traps. In Proc. 6th International Society for Veterinary Epidemiology and Economics. Ottawa, 12-16 August. Canadian Medical Veterinary Association, Ottawa, 26-31.

Carpenter, T.E. (1980) Economic evaluation of *Mycoplasma meleagridis* infection in turkeys: I. Production losses. II. Feasibility of eradication. *Dissertation Abstracts International* 41B(2), 485.

Carpenter, T.E., Miller, K.F., Gentry, R.F., Schwartz, L.D. and Mallinson, E.T. (1979) Control of *Mycoplasma gallisepticum* in commercial laying chickens using artificial exposure to Connecticut F strain *Mycoplasma gallisepticum*. *Proceedings of the United States Animal Health Association* 83, 364–370.

Charles Perrings, Carlos Castillo-Chavez, Gerardo Chowell (2014). - Merging Economics and Epidemiology to Improve the Prediction and Management of Infectious Disease *EcoHealth* 11, 464–475, 2014 DOI: 10.1007/s10393-014-0963-6

Davidson J. N. , Carpenter T. E. & Hjerpe C.A. (1981). - An example of an economic decision analysis approach to the problem of thrombo-embolic meningo-encephalitis (TEME) in feedlot cattle. *Cornell Vet.*, 71 (4), 383-390.

Dijkhuizen A.A., Renkema J.A. & Stelwagen J. (1991).-Modelling to support animal health control. *Agric. Econ.*, 5 (3), 263-277.

Dijkhuizen, A.A. and Morris, R.S. (eds) (1997) *Animal Health Economics: Principles and Applications*. University of Sydney, Postgraduate Foundation in Veterinary Science, Sydney, Australia.

Dijkhuizen, A.A., Huirne, R.B.M. and Jalvingh, A.W. (1995) Economic analysis of animal diseases and their control. *Preventive Veterinary Medicine* 25, 135–149.

Ellis, P.R. (1972a) An Economic Evaluation of the Swine Fever Eradication Programme in Great Britain, Using Cost–Benefit Analysis Techniques. Study No. 11, Department of Agriculture, Reading University, Reading, UK, 77 pp.

Ellis, P.R. (1972b) The veterinarian's contribution to the task of increasing world beef supplies. *Veterinary Record* 91(22), 530–532.

Ellis, P.R., James, A.D. and Shaw, A.P.M. (1977) Studies on the Epidemiology and Economics of Swine Fever Eradication in the EEC. EUR 5738, Commission of the European Communities, Brussels, 90 pp.

Fenichel E (2013) Economic considerations for social distancing and behavioral based policies during an epidemic. *Journal of Health Economics* 32:440–451

Helena Hansson (2019).Modelling animal health as a production factor in dairy production - a case of Swedish dairy agriculture Advanced level Agricultural Programme- Economics and Manegment Degree thesis No 1189 ISSN 1401-4084 Uppsala 2019

Hugh-Jones, M.E., Ellis, P.R. and Felton, M.R. (1975) An Assessment of the Eradication of Bovine Brucellosis in England and Wales. Department of Agriculture and Horticulture, University of Reading, Reading, UK, 75 pp.

Hurd H.S. & Kaneene J.B. (1993). - The application of simulation models and systems analysis in epidemiology: a review. *Prev. vet. Med.*, 15 (2-3), 81-99.

Keyns, D. M. Obschaya teoriya zanyatosti, protsenta i deneg / D. M. Keyns. – Moskva : Direkt-Media, 2014. – 405 s. – Rezhim dostupa: po podpiske. – URL: <https://biblioclub.ru/index.php?page=book&id=26818> (data obrascheniya: 22.09.2021). – ISBN 978-5-4460-9467-7. – Tekst : elektronnyiy.<https://biblioclub.ru/index.php?page=book&id=26818>

Makovska I., Zhukovskiy M., Nedosekov V. (2020). EkonomIchnI aspekti preventsIYi skazu tvarin. *NaukovI dopovIdI NatsIonalnogo unIversitetu bIoresursIv I prirodokoristuvannya UkraYini. №6 (88)*. <https://doi.org/10.31548/dopovidi2020.06.016>

McInerney, J.P. (1988) The economic analysis of livestock disease: the developing framework. *Acta Veterinaria Scandinavica* 84(Supplement), 66–74.

McInerney, J.P. (1996) Old economics for new problems – livestock disease: presidential address. *Journal of Agricultural Economics* 47(3), 295–314.

McInerney, J.P., Howe, K.S. and Schepers, J.A. (1992) A framework for the economic analysis of disease in farm livestock. *Preventive Veterinary Medicine* 13(2), 137–154.

Mlangwa J.E.D. and Samui K.L. (1996) The nature of animal health economics in relation to veterinary epidemiology. - *Rev. sci. tech. Off. int. Epiz.*, 1996, 15 (3), 797-812

Morris, R.S. (1999) The application of economics in animal health programmes: a practical guide. *Rev. sci. tech. Off. Int. Epiz.* 18(2), 305-314

Nedosekov V. Zhukovskiy M. (2017). Sistema fInansuvannya protiepIzootichnih zahodIv ta zabezpechennya epIzootichnogo blagopoluchchya UkraYini. *NaukovI DopovIdI NUBIP UkraYini, №4. (68)*. <http://dx.doi.org/10.31548/dopovidi2017.04.020>

- Nedosekov V., Haunhorst E., Sitnik V., Shevchuk V., Zhukovskiy M. Organizatsiya ta ekonomika veterinarnoyi spravi: navch. Posibnik. Kiyiv: NUBIP UkraYini, 2019. 408s.
- Ngategize P.K. & Kaneene J.B. (1985). – Evaluation of the economic impact of animal diseases on production: a review. *Vet. Bull.*, 55 (3), 153-162.
- Otte M.J., Chilonda P.: *Animal Health Economics: an Introduction*. Livestock Information, Sector Analysis and Policy Branch, Animal Production and Health Division (AGA), FAO, Rome, Italy. <ftp://ftp.fao.org/docrep/fao/010/ag275e/ag275e.pdf>
- Otte, M. J., Roland-Holst, D., Pfeiffer, D., Soares-Magalhaes, R., Rushton, J., Graham, J. and Silbergeld, E. (2007) *Industrial Livestock Production and Global Health Risks*. Research Report, FAO-PPLPI, Rome, Italy, with Johns Hopkins School of Public Health, Maryland, University of California, California and RVC, London.
- P. Chilonda & G. Van Huylenbroeck (2001). A conceptual framework for the economic analysis of factors influencing decision-making of small-scale farmers in animal health management. - *Rev. sci. tech. Off. int. Epiz.*, 2001, 20 (3), 687-700
- Parkin M. & King D. (1992). - *Economics*. Addison-Wesley Publishing Co., Workingham, 1027 pp.
- Perry, B., Randolph, T.F., McDermott, J.J., Sones, K.R. and Thornton, P.K. (2002) *Investing in Animal Health Research to Alleviate Poverty*. ILRI, Nairobi, Kenya, 140 pp.
- Perry, B.D., McDermott, J. and Randolph, T. (2001) Can epidemiology and economics make a meaningful contribution to national animal-disease control? *Preventive Veterinary Medicine* 48, 231–260.
- Rat-Aspert. O., Krebs. S., (2011). - An economic approach to collective management of endemic animal diseases Paper prepared for presentation at the EAAE 2011 Congress Change and Uncertainty Challenges for Agriculture, Food and Natural Resources August 30 to September 2, 2011 ETH Zurich, Zurich, Switzerland
- Renkema J.A. (1980). - Economic aspects of disease in animals, with special reference to the assessment of losses. *Bull. Off. int. Epizoot.*, 92 (5-6), 443-458.
- Rushton, J. (2006) *Animal health systems and status – Are they trade barriers or mechanisms to improve global animal disease control* In: *Proceedings of the International Agricultural Trade and Research Consortium Summer Symposium Held in Bonn, Germany 28–30 May 2006*. Available at: http://www.ilr.uni-bonn.de/iatrc/iatrc_program/Session%202/J%20Rushton.pdf
- Rushton, J. *Economics of Animal Health and Production practical and theoretical guide*. University of Liverpool, UK 2011. 384 Pages.
- Rushton, J., Thornton, P. and Otte, M.J. (1999) *Methods of economic impact assessment*. In: *The Economics of Animal Disease Control*. *OIE Revue Scientifique et Technique* 18(2), 315–338.
- Rushton, Jonathan, *Improving the use of economics in animal health – Challenges in research, policy and education*. *Preventive Veterinary Medicine* <http://dx.doi.org/10.1016/j.prevetmed.2016.11.020>
- Stott, A.W. (2005) *Costs and benefits of preventing animal diseases: a review focusing on endemic diseases*. Report to SEERAD under Advisory Activity 211. Available at: <http://www.scotland.gov.uk/library5/environment/cbpad-00.asp>
- Tisdell, C. (1968) *The Theory of Price Uncertainty, Production and Profit*. Princeton University Press, Princeton, New Jersey.
- Tisdell, C. (1995) *Assessing the Approach to Cost–Benefit Analysis of Controlling Livestock Diseases of McInerney and Others*. Paper No. 3 of *Research Papers and Reports in Animal Health Economics*, University of Queensland, Australia, 22 pp.
- Vagsholm I., Carpenter T.E. & Howitt R.E. (1991). - Simultaneous equations bias in animal production systems. *Prev. vet. Med.*, 11 (1), 37-54.
- Yustyniuk V., Nedosekov V., Kepple O., Melnyk V., Polischuk V., De Nardi M. & Correa M. (2021). – Potential paths for the introduction of risk analysis to improve the veterinary epidemiology curriculum in Ukraine. *Rev. Sci. Tech. Off. Int. Epiz.*, 39 (3). <https://www.oie.int/en/document/potential-paths-for-the-introduction-of-risk-analysis-to-improve-the-veterinary-epidemiology-curriculum-in-ukraine/>
- Zhukovskiy M. MizhnarodnI veterinarnI organIzatsIYi. NaukovI dopovIdI NatsIonalnogo unIversitetu bIoeresursIv I prirodokoristuvannya UkraYini. 2019, No6 (82). <https://doi.org/10.31548/dopovidi2019.06.018>
- Zhukovskiy M.O., Misnichenko V.I., Nedosekov V.V. Analiz mizhnarodnoho dosvidu finansuvannya protyepizootychnykh zakhodiv / Naukovi dopovidi Natsionalnoho universytetu bioresursiv i pryrodokorystuvannya Ukrainy, 2016, № 1 (58) – Rezhym dostupu: http://nd.nubip.edu.ua/2016_1/index.html (data zvernennia 2.06.2017 r.).
- Zhukovskiy, M. O. (2018). *Financing of antiepidemiologic measures in the EU countries. Opportunities for Ukraine*. [Finansuvannya protyepizootychnykh zakhodiv v krainakh ES. Mozhlyvosti dlia Ukrainy].

Scientific Reports of the National University of Life and Environmental Sciences of Ukraine 6, (76).
<https://doi.org/10.31548/dopovidi2018.06.024>

Zhukovskyi, M.O, Nedosekov, V.V, Perotskaya, L.V, & Pivovarova, I.V (2019). The experience of EU countries in financing anti-epizootic measures and compensation in emergencies. [Dosvid krain ES u finansuvanni protyepizootychnykh zakhodiv ta kompensatsii za emerzhentnykh sytuatsii]Agrarian Bulletin of the Black Sea Region, 58–66.

Zhukovskyi, M.O, Nedosekov, V.V. Evolution of animal health economy. NaukovI dopovIdI NatsIonalnogo unIversitetu bIoresursIv I prirodo koristuvannya UkraYini. №3 (91), 2021
<http://dx.doi.org/10.31548/dopovidi2021.03.008>