DOI: 10.29326/2304-196X-2021-10-4-342-348

Prospects for the use of a *Bacillus subtilis* metabolites-based feed additive in dairy farming

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SUMMARY

Laboratory and field experiment on use of the feed additive based on *Bacillus subtilis* endo- and exometabolites for the cows in different physiological periods is described in the paper. The feed additive impact on main body systems of the tested cows ($n = 30$), milk production parameters, growth rate of the calves ($n = 18$) born to the said cows were examined. The feed additive was added to the diets for the cows of test groups, 15 g per cow. The feed additive was found to have a positive effect on immunohematological and metabolic processes in postpartum cows. Neutrophils' phagocytic activity increased by 12.5 and 14.6% in the animals of test group 1 and test group 2, respectively, as compared to that one in control animals (42.8 ± 1.9%). Neutrophil absorbency increased by 2.5 times, 3.2 times and 2.1 times in the animals of test group 1, test group 2 and control group, respectively. The proportion of T-lymphocytes in blood of animals in test group 1 and test group 2 was 44.5 and 48.9%, respectively, proportion of T-lymphocytes in blood of control animals equaled to 37.5%. Trend for increase in total protein concentration in cow sera owing to increase in albumin fraction was observed in postpartum period: it was 72.91 ± 3.45 g/L in test group 1; 75.54 ± 4.12 g/L in test group 2; 70.95 ± 4.25 g/L in control group. Average daily milk yield in cows of test group 1, test group 2 and control group for 150 days of lactation was 24.50 ± 1.86 kg; 25.33 ± 1.45 kg and 22.75 ± 4.41 kg, respectively. Higher growth rate was reported for the calves born to the cows received the diet supplemented with the said feed additive. Heifers of test group 1 and test group 2 have reached body weight of 193.51 ± 5.76 and 195.33 ± 3.76 kg and in control group – of 187.33 ± 4.98 kg within 6 months. Feed additive based on endo- and exometabolites of *Bacillus subtilis* is recommended for cow diets for high-yielding dairy herd creation and food-producing animal health maintenance.

Keywords: dairy farming, feed additive, *Bacillus subtilis*, immunohematology, biochemistry daily body weight gain

Acknowledgements: The studies were performed with the financial support of the Ministry of Education and Science of the Russian Federation within the framework of the Program of Fundamental Research at the State Scientific Academies for 2013–2020 using "Molecular, Biological and Nanobiotechnological Techniques for the Development of Next Generation Biologicals, Technologies and Methods of Their Use to Control Highly Dangerous Infectious, Parasitic and Non-Contagious Animal Diseases".

For citation: Malkov S. V., Krasnoperov A. S., Poryvaeva A. P., Oparina O. Yu., Belousov A. I., Brilliant A. N. Prospects for the use of a *Bacillus subtilis* metabolites-based feed additive in dairy farming. *Veterinary Science Today*. 2021; 10 (4): 342–348. DOI: 10.29326/2304-196X-2021-10-4-342-348.

Conflict of interest: The authors declare no conflict of interest.

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УДК 619:636.085.57:615.331:636.034

Перспективы применения кормовой добавки на основе метаболитов *Bacillus subtilis* в молочном животноводстве

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РЕЗЮМЕ

Представлены результаты научно-производственного опыта применения кормовой добавки на основе эндо- и экзометаболитов *Bacillus subtilis* коровам в разные физиологические периоды. Изучено ее влияние на функционирование основных систем организма подопытных животных ($n = 30$), показатели молочной продуктивности, интенсивность роста родившихся от них телят ($n = 18$). Коровам из опытных групп вводили в рацион кормовую добавку в дозе 15 г в сутки на 1 голову. Установлено, что кормовая добавка оказывает положительное влияние на нормализацию иммуногематологических и метаболических процессов у коров в послеродовой период. Показатель фагоцитарной активности нейтрофилов у животных 1-й опытной группы увеличился на 12,5%, 2-й опытной группы – на 14,6% по сравнению с контрольной группой (42,8 ± 1,9%). Поглотительная способность нейтрофилов у особей 1-й опытной группы увеличилась в 2,5 раза, 2-й опытной группы – в 3,2 раза, контрольной группы – в 2,1 раза. Содержание относительного количества Т-лимфоцитов в крови животных 1-й и 2-й опытных групп регистрировали на уровне 44,5 и 48,9% соответственно, у особей контрольной группы данный показатель был равен 37,5%. В послеродовой период отмечали тенденцию к увеличению концентрации общего белка в сыворотке крови коров за счет повышения альбуминовой фракции: в 1-й группе – 72,91 ± 3,45 г/л; во 2-й группе – 75,54 ± 4,12 г/л; в контрольной группе – 70,95 ± 4,25 г/л. Установлено, что за 150 дней лактации среднесуточный удой у коров 1-й группы составил 24,50 ± 1,86 кг; 2-й группы – 25,33 ± 1,45 кг; контрольной группы – 22,75 ± 4,41 кг. Зарегистрирована более высокая интенсивность роста телят, рожденных от коров, которым в основной рацион вводили кормовую добавку. Телочки 1-й и 2-й опытных групп за 6 мес. достигли живой массы тела, равной 193,51 ± 5,76 и 195,33 ± 3,76 кг, а особи контрольной – 187,33 ± 4,98 кг. В целях реализации задачи по созданию высокопродуктивного молочного стада и сохранения биологического благополучия сельскохозяйственных животных-продуцентов кормовая добавка на основе комплекса эндо- и экзометаболитов *Bacillus subtilis* рекомендована к применению в рационах кормления коров.

Ключевые слова: молочное животноводство, кормовая добавка, *Bacillus subtilis*, иммуногематология, биохимия, среднесуточный прирост живой массы тела

Благодарности: Работа выполнена при финансовой поддержке Минобрнауки России в рамках Программы фундаментальных научных исследований государственных академий наук на 2013—2020 гг. по направлению «Молекулярно-биологические и нанобиотехнологические методы создания биопрепаратов нового поколения, технологии и способы их применения с целью борьбы с особо опасными инфекционными, паразитарными и незаразными болезнями животных».

Для цитирования: Малков С. В., Красноперов А. С., Порываева А. П., Опарина О. Ю., Белоусов А. И., Бриллиант А. Н. Перспективы применения кормовой добавки на основе метаболитов *Bacillus subtilis* в молочном животноводстве. *Ветеринария сегодня*. 2021; 10 (4): 342–348. DOI: 10.29326/2304-196X-2021-10-4-342-348.

Конфликт интересов: Авторы заявляют об отсутствии конфликта интересов.

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INTRODUCTION

Dairy livestock farming is currently one of the fast-paced agricultural subsectors in the Russian Federation. The said subsector development, improvement and economic efficiency as for satisfying dairy product needs of the country's population should be largely fostered by the state support mechanisms optimization, investment attracting, technological efficiency and herd performance improvement [1, 2]. The main way of milk production ramp-up is sustainable management of the animals with world-class genetic potential and raising of high-yielding dairy cows, development and usage of physiologically adequate and economically sound feed preparation and feeding schemes [3, 4].

Increase in domestic milk production driven by animal performance improvement and creating enabling environment for their genetic potential realization is the task that is getting more urgent every day due to dairy cattle population reduction in our country. At the same time, determination of milk and dairy products safety indicators remains urgent for maintaining the national human population health.

Systematic dairy farming development is intimately associated with the designing a system for animal performance improvement as well as for animal health protection. All kinds of methods including application of different products that are not always environmentally-friendly are used for this purpose. Therefore, biotechnological methods and tools for animal farming industry modernization are being increasingly put into practice, especially those associated with use of new feed additives developed on the basis of prebiotics and metabiotics [5, 6]. Metabiotic feed additives contain metabolites or structural components of probiotic microorganisms. Metabiotics stimulate selectively the growth and biological activity of normal gut microbiota. They are targeted to gut functioning normalization through stabilizing effect on the microbiota and eubiosis support, they optimize metabolism and immunity processes that ultimately should result in an increase in animal performance and product quality [6–8].

Table 1
Design of laboratory and production experiment in cows

Group of animals	Experiment design
Test group 1 ($n = 10$)	Basic diet + 15 g of the feed additive administered to each cow for 14 days before calving
Test group 2 ($n = 10$)	Basic diet + 15 g of the feed additive administered to each cow for 14 days before calving and for 14 days after calving
Control group ($n = 10$)	Basic diet

Development and introduction of new domestic feed additives based on bacterial cell metabolites capable of maintaining controlled gut microbiocenosis and not interfering with gut microbiota that are easily producible and stable during their storage is the main task for researchers and developers in biotechnological industry [6, 7, 9].

The study was aimed at testing of feed additive based on *Bacillus subtilis* endo- and exometabolites for its effect on cow main body systems' functioning and cow milk yields as well as on their offspring weight gain rate.

MATERIALS AND METHODS

The study was performed in the Laboratory for Immunology and Pathobiochemistry of the Ural Research Veterinary Institute of the FSBSI UrFASRC, UrB of RAS and in one agricultural holding located in the Ural Federal District in spring-summer period and in summer-autumn period in 2019.

Second- and third-lactation Russian black pied cows with at least 75% Holstein genetics ($n = 30$) and heifers born to them ($n = 18$) were used for the study.

The tested feed additive contained a complex of *Bacillus subtilis* endo- and exometabolites (proteins, amino acids, enzymes, antibiotic substances, structural components of destroyed bacterial cells, etc.).

The following analogues groups of animals were formed for laboratory and field experiment: two test and one control group, 10 cows in the same physiological state – in late dry period per group. All animals were apparently healthy, kept in one holding facility and fed on the diet used in the said holding. Cows of both test groups were fed individually with tested feed additive in addition to the basic diet. The period when the cows were fed with the feed additive (14 days before and after calving) was determined based on the period of maximum metabolic load on the animals' body [10]. Design of laboratory and field experiment is given in Table 1.

The cows were daily observed for their physiological state for 150 days. Control milkings were performed monthly starting from day 15 after calving to assess the milk yields. Milk fat mass fraction was determined with 'CombiFoss FT+' automatic analyzer (Foss, Denmark).

Blood samples for laboratory tests were collected thrice to vacuum tubes; on day 1 after calving (background), 14 and 28 days after calving in morning hours before feeding.

The experiments in animals were carried out in accordance with the Declaration of Helsinki (2000) and Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on protection of animals used for scientific purposes.

Complete blood count was performed with 'Abacus Junior Vet' hematology analyzer (Diatron, Austria) using standard reagents (Diatron, Austria); white cell count was measured in Romanowsky-Giemsa-stained blood smears (300 cells per smear) under 'Olympus BX 43' microscope (Olympus, Japan). Immunological tests of blood comprised tests for relative T- and B-lymphocyte content, T/B index, phagocyte index (PI), phagocytic activity (PA) of neutrophils and monocytes according to P. N. Smirnov et al. (2007) [11]. The reaction results were viewed under MC 100 (XP) binocular microscope (Micros, Austria) and recorded. Biochemical tests including turbidimetry, colorimetry and kinematic analysis were carried out with 'Chem Well-2910 Combi' analyzer (Awaveness Technology, USA) using original reagent panels (Vital Diagnostics SPb, Russia; DIALAB GmbH, Austria). The reliability of the performed measurements was confirmed by tests of reference materials recommended by the reagent manufacturers.

Three groups of heifers were formed for tests for body weight gains in the offspring of the cow dams involved in the laboratory and field experiment. The design of the test of calves for their body weight gains is given in Table 2.

Arithmetic mean and standard deviation were calculated for all values and expressed as $\bar{x} \pm s.d.$ Calculations and graph plotting were performed with PAST (version 4.05) and MS Excel 2016 packages.

Table 2
Design of the test of heifers for body weight gains

Group of animals	Animal characteristics	Feeding			Frequency of individual weighing
		day 1–5	day 6–15	day 16 and onwards	
Test group 1 ($n = 6$)	Heifers born to the cows of test group 1	Heifers were individually fed thrice with their dams' colostrum	Heifers were individually fed with milk from their dams	Pooled whole milk and basic diet for young animals	At birth; at the age of one month; at the age of two months; at the age of three months; at the age of four months; at the age of five months; at the age of six months.
Test group 2 ($n = 6$)	Heifers born to the cows of test group 2				
Control group ($n = 6$)	Heifers born to the cows of control group				

RESULTS AND DISCUSSION

The background tests of the cows of test groups and control group for main morphological blood gradients demonstrated their compliance with standard values for the postpartum period without significant intergroup differences. Tests of blood samples collected from the cows 14 and 28 days after calving showed that erythrocyte, hemoglobin, leukocyte, lymphocyte, platelet counts were variable but were within the normal limits. Dynamics of hematological indicators correlated with hematopoiesis normalization in cows in postpartum period. The experiment findings correlated with data of other researchers [12, 13].

Analysis of the cellular component of the immune system showed that monocyte-macrophage phagocytic activity had increased by day 28 of the experiment as evidenced by increased absorption capacity of phagocytic cells. Neutrophils' phagocytic activity increased by 12.5% (test group, PA 55.32 ± 1.31%) and 14.6% (test group 2, PA 57.44 ± 1.72%) in tests animals, as compared to that one in control animals (PA 42.80 ± 1.91%). Enhanced neutrophil absorbency was reported in animals of all groups but its dynamics was different. In test group 1, phagocytic index increased by 2.5 times as compared to background one and averaged to 9.61 ± 0.54 c. u. In test group 2, phagocytic index increased by 3.2 times (11.82 ± 1.14 c. u.), and in animals of control group phagocytic index increased by 2.1 times (8.21 ± 0.76 c. u.). Relative T-lymphocyte content in blood of animals of test group 1 and test group 2 were 44.5 and 48.9%, respectively, that was correlated to standard physiological parameters (40–60%). Relative T-lymphocyte content in control animals were 37.5%.

T/B-lymphocyte index in animals of test group 1 and test group 2 was 1.51 ± 0.12 and 2.22 ± 0.09 c. u., respectively, that was indicative of the balance between cellular and humoral immunity components. In control animals humoral immunity component slightly prevailed by day 28 of the experiment, T/B-lymphocyte index was 1.39 ± 0.07 c. u.

Thus, it could be supposed that the feed additive administration had an indirect positive impact on hematopoiesis normalization and natural resistance stabilization in postpartum cows.

Analysis of changes in biochemical parameters in cows of all group after calving revealed a trend for increase in total protein concentration in cow sera owing to increase in albumin fraction. Total protein concentration was 72.91 ± 3.45 g/L in test group 1; 75.54 ± 4.12 g/L in test group 2; 70.95 ± 4.25 g/L in control group by day 28 of the experiment (Figure 1).

Slight fluctuations in cholesterol and triglyceride levels within the reference limits were observed in cows of all groups when their lipid metabolisms were assessed. Thus, in cows cholesterol level was not more than 3.2 mmol/L, triglyceride levels were in the range of 0.2–0.3 mmol/L.

It was also important that alkaline phosphatase enzymatic activity values were positive in cows of test groups. Alkaline phosphatase level was by 20.56% and 29.46% lower in cows of test group 1 and test group 2 as compared to that one in cows of control group on day 28 of the experiment. Aspartate aminotransferase (AsAT) activity in cows of all groups was within the reference limits. Detected changes were indicative of total decrease in toxic load on the cows' hepatobiliary system in the postpartum period.

Mineral metabolism intensity was assessed based on dynamics of calcium and phosphorous levels in cow sera. Thus, cumulative calcium and phosphorous values in sera of test group 1 and test group 2 cows were averagely by 5.66 and 6.67% higher than that ones in cows of control group (Figure 1).

It could be supposed that some variability in blood immunobiochemical parameters in cows of test groups were associated with indirect positive impact of the feed additive that was correlated with some research results [2, 12].

Moreover, the additive was noted to have positive effect on accumulation of the significant energy required for animal health and performance maintaining. This was

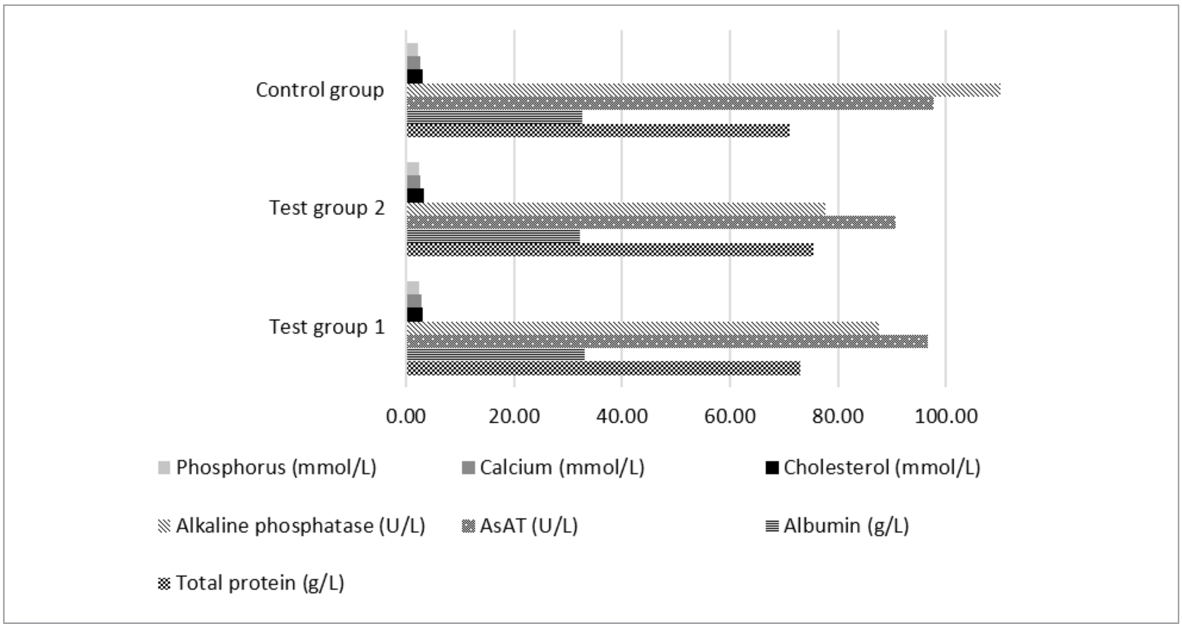

Fig. 1. Biochemical parameters on day 28 of experiment

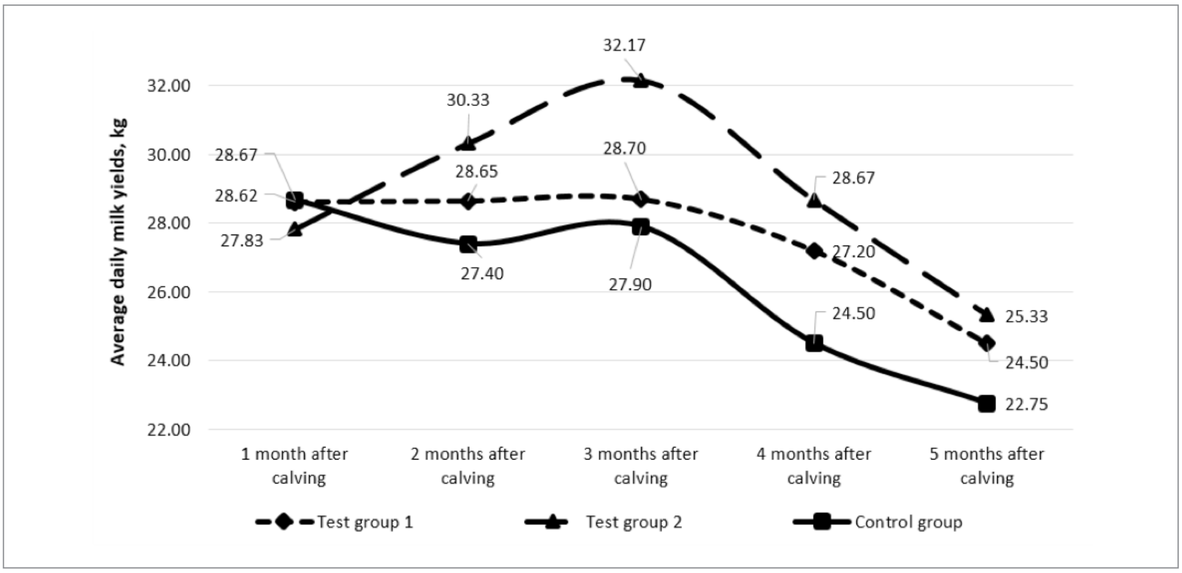

Fig. 2. Dynamics of average daily milk yields (kg) during the experiment

supported by the data on cows' milk yields for the whole test period.

Figure 2 shows graphs of milk yields in all groups. The highest milk yields were registered by day 90 of lactation. Average daily milk yields in cows of test group 1, test group 2 and control group were 28.70 ± 2.65 kg; 32.17 ± 1.92 kg and 27.90 ± 3.24 kg, respectively.

The following average daily milk yields were registered in test group 1, test group 2 and control group by the end of the experiment: 24.50 ± 1.86 kg; 25.33 ± 1.45 kg; 22.75 ± 4.41 kg, respectively.

Milk production levels in the cows fed the diet supplemented with the feed additive remained higher than that ones in the cows of control group during the whole test period starting with the second month after calving.

Mass fraction of protein is an important criterion for milk quality evaluation. The mass fraction of protein varied within the range of 2.85–3.38% during the whole experiment period. The average mass fraction of protein in control group, test group 1, test group 2 was 3.01, 3.03, and 3.27%, respectively, proved the feed additive positive effect on milk quality.

In the view of modern technologies introduced in dairy farming, replacement heifer raising under controlled conditions is of great importance for high-yielding dairy herd creation. It could be achieved through increase in young animals' body weight gain rates that are directly associated with future milk yields [14].

Therewith, average daily body weight gains of future replacement heifers born to the cows fed the feed additive were determined (Figure 3).

The calves born to the cows fed with the feed additive in dry and postpartum periods developed more intensively in the first months of their lives than others under similar

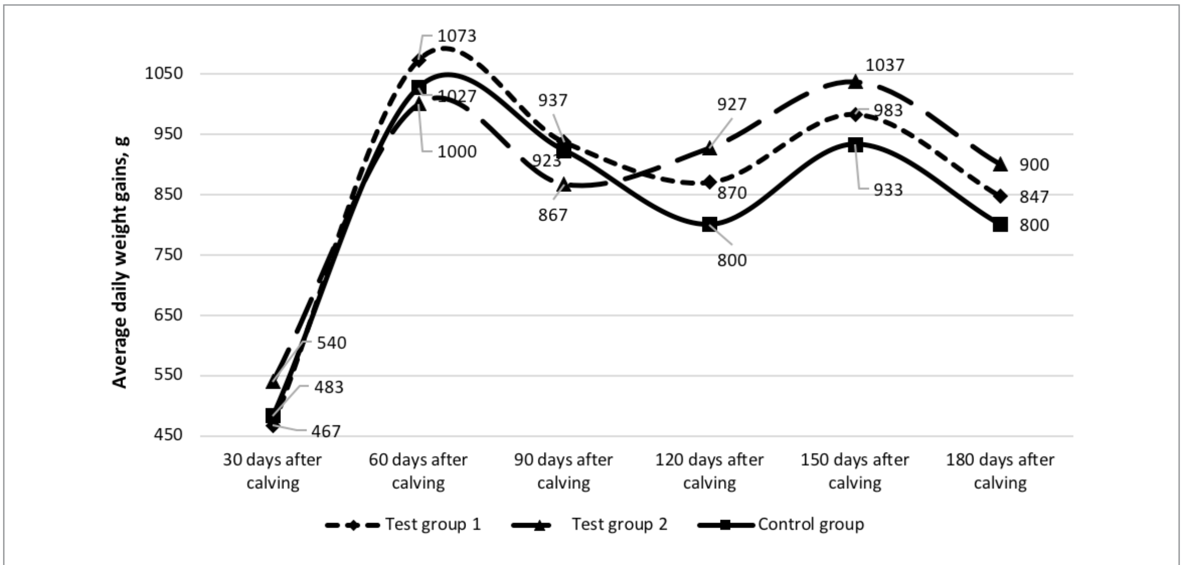

Fig. 3. Dynamics of average daily body weight gains (g) in heifers

feeding and keeping conditions. Average body weight of newborn calves born to the test and control cows was 37.91 ± 1.24 kg. Then, high body weight gain rate was reported in heifers born to the dams fed with a diet supplemented with the feed additive. Thus, the heifers born to the cows of test group 1 and test group 2 had reached body weight of 193.51 ± 5.76 and 195.33 ± 3.76 kg, respectively, for 6 months and the heifers born to control cows had reached body weight of 187.33 ± 4.98 kg for 6 months.

Weight gains in heifers of test groups were higher than that ones in control group during the whole experiment period that confirmed the positive feed additive impact on young animals' growth rate.

The first 6 months of life are proved to be the most important for the internal organ development and functional adjustment, for the development of the ability to absorb nutrients from various feed components, that have indirect impact on the future animal's milk production and growth rate [15, 16]. The experiment data can be accounted for the feed additive positive impact including dams' metabolism normalization, easier calving, more viable less disease-susceptible offspring with more efficient diet nutrient intake. The results of the study are correlated with the data of some authors [17–19].

CONCLUSION

Promising use of *Bacillus subtilis* metabolite complex-based feed additive in dairy farming was demonstrated in the laboratory and field experiment. The said feed additive was shown to have positive impact on cows' hematopoietic and metabolic processes. Thus, blood immunohematological and biochemical parameters had been restored and normalized by day 25–28 regardless of the scheme of the tested feed additive administration to experimental animals in the postpartum period. Protein, lipid and mineral metabolism indicators in the cows of test groups were at the upper normal limit. Analysis of metabolic indicators of hepatobilliary system state showed that the toxic load on parenchymal organs of test animals was minimal on day 28.

Tested *Bacillus subtilis* metabolite complex-based feed additive has a prolonged corrective effect on the cows' intestinal eubiosis manifested by effective diet nutrient absorbance and digestibility. This was confirmed by average daily milk yields in cows of test group 1 and test group 2 that were 24.50 ± 1.86 and 25.33 ± 1.45 kg as compared to that ones in cows of control group that were 22.75 ± 4.41 kg.

Feeding of the heifers born to the feed additive-fed dams with their colostrum and milk had a positive impact on the heifers growth rates (average daily body gains in the heifers born to cows of test group 1 and test group 2 were 862 g and 878 g, respectively; average body weight of the test group 1 and test group 2 at the age of 6 months was 193.51 ± 5.76 kg and 195.33 ± 3.76 kg, respectively).

For creation of a high-yielding dairy herd and maintaining of food-producing animal health it is recommended to use *Bacillus subtilis* endo- and exometabolites-based feed additive in the diets for the cows: 1) in late dry period – at a dose of 15 g/animal for 14 days before calving; 2) in postpartum period for prevention metabolic disorders, general resistance correction and performance improvement – at a dose of 15 g/animal for 14 days after calving.

REFERENCES

1. Stolyarova O. A., Stolyarova Yu. V. Improving public support of dairy cattle breeding in the region. *Regional Economics: Theory and Practice*. 2017; 15 (6): 1148–1161. DOI: 10.24891/re.15.6.1148. (in Russ.)

2. Belousov A. I., Sokolova O. V., Bespamyatnykh E. N. The use of biochemical screening in assessing the productive health of high-yielding cows in the Sverdlovsk Region. *Issues of Legal Regulation in Veterinary Medicine*. 2018; 4: 278–280. DOI: 10.17238/issn2072-6023.2018.4.278. (in Russ.)

3. Gorelik V. S., Tairova A. R., Kharlap S. Yu. The effectiveness of the use of drugs of Chitosan in dairy cattle breeding. *Feeding of agricultural animals and feed production*. 2016; 2: 17–22. Available at: https://panor.ru/articles/effektivnost-ispolzovaniya-preparatov-khitozana-v-molochnom-skotovodstve/68596.html. (in Russ.)

4. Subbotina N. A., Morozova L. A., Mikolaychik I. N. Increasing the milk yield of cows on rations enriched by feed additive Megalac. *Feeding of agricultural animals and feed production*. 2016; 8: 39–46. Available at: https://panor.ru/articles/razdoy-korov-na-ratsionakh-obogashchennykh-kormovoy-dobavkoy-megalak/69441.html. (in Russ.)

5. Suresh G., Cabezudo I., Pulicharla R., Cuprys A., Rouissi T., Brar S. K. Biodegradation of aflatoxin B_1 with cell-free extracts of *Trametes versicolor* and *Bacillus subtilis*. *Res. Vet. Sci*. 2020; 133: 85–91. DOI: 10.1016/j.rvsc.2020.09.009.

6. Ardatskaya M., Stolyarova L., Arkhipova E., Filimonova O. Yu. Metabiotics as a natural development of a probiotic concept. *Difficult Patient*. 2017; 15 (6–7): 35–39. Available at: https://t-pacient.ru/articles/9652. (in Russ.)

7. Plotnikova E. Yu., Gracheva T. Yu. Metabiotics – the complex solution of dysbiotic problems at various diseases. *RMJ*. 2018; 26 (5–2): 72–76. Available at: https://www.rmj.ru/articles/pediatriya/Metabiotiki_kompleksnoe_reshenie_disbioticheskih_problem_pri_razlichnyh_zabolevaniyah (in Russ.)

8. Chervinets Yu. V., Chervinets V. M., Shenderov B. A. Modern concept on the biotechnological potential of symbiotic human microbiota. *Upper Volga Medical Journal*. 2018; 17 (1): 19–26. Available at: http://medjournal.tvergma.ru/id/eprint/355. (in Russ.)

9. Yakovenko E. P., Agafonova N. A., Yakovenko A. V., Ivanov A. N., Soluyanova I. P. Antibiotics, prebiotics, probiotics, metabiotics in the therapy of small intestinal bacterial overgrowth. *Difficult Patient*. 2018; 16 (4): 16–22. Available at: https://t-pacient.ru/articles/9836/. (in Russ.)

10. Fomichev Yu. P., Gusev I. V., Sulima N. N., Ermakov I. Yu. Effectiveness of feed additives on cow metabolism and milk productivity. *Fodder Journal*. 2018; 1: 40–48. DOI: 10.25685/KRM.2018.2018.9953. (in Russ.)

11. Panel' naibolee informativnykh testov dlya otsenki rezistentnosti zhivotnykh: metodicheskie rekomendatsii = Panel of the most informative tests of animals for resistance: methodical guidelines. Prepared by P. N. Smirnov et al. Novosibirsk.; 2007; 37 p. eLIBRARY ID: 19495039. (in Russ.)

12. Chabaev M. G., Nekrasov R. V., Kumarin S. V., Zelenchenkova A. A., Vinogradov V. N., Savushkin V. A., et al. Effect of feeding probiotics on the basis of spore-forming bacteria on metabolism and productive traits in milky calves and calved cows. *Problems of Productive Animal Biology*. 2016; 2: 55–65. Available at: http://bifip.ru/zhurnal/

arkhiv/item/vliyanie-skarmlivaniya-probiotikov-na-osnove-sporoobrazuyushchikh-bakterij-na-produktivnost-i-obmen-veshchestv-u-telyat-molochnikov-i-novotelnykh-korov. (in Russ.)

13. Rastorguyeva S. L., Ibishov D. F., Osipov A. P. Integrated effect of the Vitadaptin, the Guvitan-C, and the Germiviti on the absolute level of leukocytes, lymphocytes, and neutrophils in the peripheral blood of dry cows. *Perm Agrarian Journal*. 2019; 2 (26): 136–142. Available at: http://agrovest.psaa.ru/wp-content/uploads/2019/08/agrar_vest-2-26.pdf. (in Russ.)

14. Nekrasov R. V., Chabaev M. G., Zelenchenkova A. A., Suslova I. A., Kartashov M. I., Rogowskiy S. V. Productivity cattle at enrichment diets probiotic. *Dairy and Beef Cattle Farming*. 2016; 7: 19–22. eLIBRARY ID: 28091505. (in Russ.)

15. Shatskikh E., Barmina I. The milk productivity of cows of holstein black-and-white breed of american selection under conditions of middle Urals. *Glavnyi zootekhnik*. 2016; 11: 3–8. eLIBRARY ID: 27277510. (in Russ.)

16. Lyubimov A. I., Asimova G. V., Malkov A. N. Use of the drug "Vetom 1.1" in the prevention of diarrhea in calves. *Agrarnaya Rossiya*. 2016; 5: 8–9. DOI: 10.30906/1999-5636-2016-5-8-9. (in Russ.)

17. Pleshkov V. A. Probiotic feed additive "Bacell-M" in the diet of calves. *Achievements of Science and Technology of AIC*. 2018; 32 (12): 53–54. DOI: 10.24411/0235-2451-2018-11215. (in Russ.)

18. Pleshkov V. A., Smolovskaya O. V., Korobeynikova L. N. The effectiveness of the use of probiotics "Monosporin" and "Bacell" in calves rations. *Aktual'nye nauchno-tekhnicheskie sredstva i sel'skokhozyaistvennye problemy: materialy II natsional'noi nauchno-prakticheskoi konferentsii = Current scientific and technical tools and agricultural challenges: Proceeding of the II National Scientific and Practical Conference (July 5, 2019)*. Kemerovo: Kuzbasskaya GSKhA; 2019; 28–31. Available at: http://www.ksai.ru/upload/files/sborniki/other/2019/Сборник%20конференции.pdf. (in Russ.)

19. Magomedaliev I. M., Nekrasov R. V., Chabaev M. G., Dzhavakhiya V. V., Glagoleva E. V., Kartashov M. I., et al. Use of different concentrations of enzymesporin probiotic in feeding of growing young pigs. *Ukrainian Journal of Ecology*. 2019; 9 (4): 704–708. DOI: 10.15421/2019_813.

Received 02.07.2021
Revised 26.07.2021
Accepted 09.08.2021

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