

ABSTRACT

For the dissertation work by Zharykzhuldyz Abirbekkyzy , prepared on the topic "Clinical, Pharmacological and Immunological Substantiation of Phytopreparations for the Treatment of Calf Dyspepsia" submitted for the degree of Doctor of Philosophy (PhD) in the specialty 8D09101 – “Veterinary Medicine”

Relevance of the Research Topic

The rearing of healthy young animals and their protection against diseases and mortality remain among the primary objectives of modern livestock production. Dyspepsia is one of the most common diseases affecting neonatal animals. It may develop in 50–100% of newborn calves by the end of the first day of life, while mortality rates may reach 30–50% within 2–5 days and, in some cases, within 7–10 days after the onset of the disease. Consequently, dyspepsia causes substantial economic losses due to impaired growth and development of calves, as well as increased expenditures on therapeutic and preventive measures. Although numerous studies have addressed this issue, achieving 100% survival of young animals remains unattainable. Therefore, the development of novel diagnostic and therapeutic approaches for neonatal calf dyspepsia continues to be a promising area of veterinary research. In clinical veterinary practice, conventional antibacterial drugs used for the treatment of dyspepsia often fail to provide satisfactory therapeutic outcomes. Moreover, these agents frequently exert adverse effects on the obligate intestinal microflora and compromise the immune status of newborn calves. Consequently, increasing attention has recently been directed toward replacing antibiotics with environmentally friendly and effective alternative therapeutic agents. Thus, the introduction of innovative treatment strategies that complement rather than replace existing therapeutic and preventive measures represents one of the most promising directions in practical veterinary medicine.

Currently, medicinal plants have attracted considerable interest among researchers and veterinary specialists. Despite the continuous development of new pharmaceuticals, the demand for herbal medicines remains consistently high. Plant-derived preparations constitute approximately 30–40% of the current pharmaceutical arsenal and account for up to 70% in certain therapeutic categories. Their major advantage over many synthetic drugs lies in the presence of diverse biologically active compounds that exert complex and multifaceted effects on the organism. Since the medicinal parts of plants contain a wide spectrum of pharmacologically and biologically active compounds, comprehensive investigation of their mechanisms of pharmacological action is of considerable scientific importance. The rational application of herbal preparations in veterinary practice has the potential to reduce the incidence of animal diseases, improve livestock survival, decrease the costs associated with expensive chemotherapeutic agents, and enhance livestock productivity. Considering these factors, the development and practical application of highly effective phytopreparations for the prevention and treatment of calf dyspepsia represent an important and relevant challenge in modern veterinary science.

The purpose of the dissertation research: The main objective of this research was to develop and scientifically substantiate highly effective, environmentally friendly, and economically feasible phytopreparations derived from locally available medicinal plant materials for the prevention and treatment of calf dyspepsia.

Research objectives:

1. To prepare phytopreparations from medicinal plant materials and to determine their pharmacotoxicological and microbiological properties, as well as their optimal therapeutic dosages.
2. To evaluate the effects of the phytopreparations on lipid peroxidation processes and the activity of the antioxidant defense system in the blood plasma of calves affected by dyspepsia.
3. To assess the effects of the phytopreparations on the clinical condition of calves with dyspepsia and on the humoral immunity indicators of the nonspecific resistance of the calf organism.
4. To investigate the effects of phytopreparations prepared from a combination of medicinal plants on the cellular immunity parameters of the nonspecific resistance in calves.
5. To evaluate the comparative prophylactic and therapeutic efficacy of the phytopreparations against calf dyspepsia.

Research Results.

Phytopreparations (infusions, extracts, and mixtures) were prepared from medicinal plant materials using a specialized technological procedure. Their pharmacological properties were investigated, and the experimental results confirmed the absence of toxic effects. The phytopreparations demonstrated pronounced antibacterial activity against various opportunistic pathogenic microorganisms. In particular, they inhibited the growth of *Escherichia coli*. The study revealed that the phytopreparations exhibited bactericidal activity against *Escherichia coli*, *Salmonella Typhimurium*, and *Staphylococcus aureus* at a dilution of 1:160, while bacteriostatic activity was observed at a dilution of 1:320. Based on the experimental findings, the optimal therapeutic doses for the treatment of calf dyspepsia were established as 5.0 mL/kg for the combined herbal mixture and 3.0 mL/kg for the combined herbal extract.

The obtained results demonstrated that the phytopreparations markedly reduced the intensity of lipid peroxidation in the blood plasma of calves affected by dyspepsia. The most pronounced effect was observed in the group treated with the combined phytopreparation. During the experimental period, the levels of lipid peroxidation products decreased by 29.3–50.5%, diene conjugates by 30.0–58.2%, and malondialdehyde by 21.3–50.5% relative to baseline values. Compared with the control group, the reductions were 16.1–26.6%, 13.6–25.5%, and 13.9–27.4%, respectively. Furthermore, the phytopreparations significantly enhanced the activity of the major components of the antioxidant defense system, increasing ceruloplasmin concentration by 22.3–50.6% and vitamin E levels by 19.0–40.0%.

The experimental data also demonstrated that calves with dyspepsia exhibited significantly lower immunological indicators of nonspecific resistance than clinically healthy animals. Clinical examination showed that, by the 5th and 10th

days after the initiation of treatment, all clinical parameters, including body temperature, pulse rate, and respiratory rate, had returned to physiological values. In all experimental groups receiving phytopreparations, morphological, biochemical, and immunological parameters were significantly higher than both baseline and control values. Specifically, erythrocyte counts increased by 15.7–21.3%, leukocyte counts by 8.5–16.3%, hemoglobin concentration by 16.9–24.6%, total protein by 10.9–20.0%, calcium by 7.5–16.0%, inorganic phosphorus by 4.9–8.9%, albumin by 11.3–16.8%, γ -globulins by 15.4–18.3%, IgA by 13.4–17.9%, IgM by 16.7–21.1%, and IgG by 18.8–23.3%.

Administration of the combined herbal extract significantly improved humoral immunity compared with the control group, increasing serum bactericidal activity by 20.4–34.0%, serum lysozyme activity by 15.4–19.0%, complement activity by 14.2–25.0%, and β -lysine activity by 21.9–34.2%. In addition, the phytopreparations exerted a stimulating effect on cellular immunity and nonspecific resistance. The most pronounced changes were observed in calves treated with the combined extract. Compared with the control group, leukocyte phagocytic activity increased by 13.4–16.6% in spontaneous assays and by 13.8–23.7% in induced assays; neutrophil phagocytic activity increased by 18.0–25.6%, while the phagocytic index increased by 12.3–18.8%. Relative to baseline values, spontaneous and induced leukocyte phagocytic activity increased by 15.8–19.2% and 17.7–33.3%, respectively, whereas neutrophil phagocytic activity increased by 19.6–30.2%, and the phagocytic index by 14.0–23.8%.

The findings demonstrated the high prophylactic efficacy of the phytopreparations. No cases of disease or mortality were recorded among calves receiving the combined herbal extract, whereas in the control group seven calves (35%) developed dyspepsia, including four animals (20%) that died. The prophylactic efficacy reached 100% in the experimental group compared with 80% in the control group. Likewise, the combined herbal extract achieved 100% therapeutic efficacy, whereas therapeutic efficacy in the control group was only 70%. Moreover, recovery in the experimental group occurred 4–5 days earlier than in the control group. The phytopreparation also promoted growth performance, resulting in a 21.4% greater increase in live body weight and a 37.2% higher absolute weight gain compared with the control group.

Scientific Novelty of the Research.

For the first time, phytopreparations were developed in the departmental research laboratory from locally available medicinal plant materials—blackthorn fruits (*Fructus Prunus spinosa*), birch leaves (*Herba Betula*), and chamomile flowers (*Flores Chamomillae*)—using a specially designed technological method. Their pharmacotoxicological and microbiological characteristics, as well as the optimal therapeutic dosages, were determined through laboratory animal studies. Furthermore, for the first time, the effects of the developed phytopreparations on lipid peroxidation processes and the activity of the antioxidant defense system in the blood plasma of calves with dyspepsia were investigated. The influence of the phytopreparations on the clinical condition of calves with dyspepsia, as well as on humoral and cellular immunity parameters, was evaluated. In addition, their

comparative prophylactic and therapeutic efficacy against calf dyspepsia was established, and their economic efficiency was assessed. The scientific novelty of the research is confirmed by a utility model patent of the National Institute of Intellectual Property of the Republic of Kazakhstan (Patent No. 10270, dated March 7, 2025). Practical Significance of the Research

Practical significance of the research.

The results of the present study demonstrated that the developed phytopreparations exhibit high prophylactic and therapeutic efficacy against calf dyspepsia. Furthermore, the experimental findings confirmed that these phytopreparations stimulate both humoral and cellular components of the nonspecific immune resistance of calves. Based on these results, the developed phytopreparations are recommended for practical application under livestock farming conditions.

The findings of the dissertation may be incorporated into the educational process for students enrolled in the Veterinary Medicine educational program, used in continuing professional development courses in phytotherapy, and applied in private and commercial livestock farming enterprises.

Main Provisions Submitted for Defense

1. The technology for the preparation of phytopreparations; the determination of their acute, cumulative, and chronic toxicological characteristics, microbiological properties, and optimal therapeutic dosages.
2. The evaluation of the effects of the phytopreparations on lipid peroxidation and the activity of the antioxidant defense system in the blood plasma of calves with dyspepsia.
3. The effects of the phytopreparations on the clinical condition of calves with dyspepsia, as well as on the humoral and cellular immunity parameters of the nonspecific resistance of the organism.
4. The scientific substantiation of the comparative prophylactic and therapeutic efficacy of the phytopreparations against calf dyspepsia.

Author's Personal Contribution.

The doctoral candidate independently conducted pharmacotoxicological, microbiological, morphological, immunological, and biochemical investigations, as well as experimental studies under farm conditions, in accordance with the objectives and research tasks of the dissertation. Certain specialized analyses were carried out with the assistance of domestic and international scientific consultants.

The experimental studies presented in this dissertation were performed at the Pharmaceutical Technologies Research and Teaching Laboratory of the Department of Pharmacology and Animal Pathology, the Republican Veterinary Laboratory (Almaty Branch), the research laboratories of the University of Warmia and Mazury (Poland), and the university's Animal Clinic and vivarium. In addition, several investigations were conducted at the Laboratory of Drug Technologies of S.D. Asfendiyarov Kazakh National Medical University. Field trials were carried out on private and commercial livestock farms located in the Zhambyl, Ili, and Enbekshikazakh districts of Almaty Region, Republic of Kazakhstan.

The results of the dissertation were presented at several international scientific and practical conferences. The author published research papers in national and international scientific journals, obtained a utility model patent, received official implementation certificates confirming the introduction of the research findings into veterinary practice and the educational process, and developed methodological recommendations based on the research outcomes.

Approbation of the Research.

The results of the research were presented and discussed at meetings of the Department and at the following international scientific and practical conferences: *Current Status and Prospects for the Development of Veterinary Medicine and Animal Husbandry in the Republic of Kazakhstan*, dedicated to the 80th anniversary of Academician of the National Academy of Sciences of the Republic of Kazakhstan, Doctor of Veterinary Sciences, Professor T.S. Saiduldin (Almaty, Kazakhstan, March 15–16, 2023); *Development Trends in Pharmacology and Toxicology* (Samarkand, Uzbekistan, May 16, 2023); *Current Issues and Prospects for the Development of Modern Science* (Chişinău, Moldova, December 15, 2023); *Achievements and Development Prospects of Veterinary Therapy in New Uzbekistan*, dedicated to the 105th anniversary of Doctor of Veterinary Sciences Kh.Z. Ibragimov (Samarkand, Uzbekistan, December 15–16, 2023); *Innovative Solutions to Current Problems of Biological, Toxicological, and Radiation Safety in the Agro-Industrial Complex* (Kazan, Russian Federation, September 11–12, 2025); *Modern Approaches to the Diagnosis, Treatment, and Prevention of Non-Infectious Animal Diseases* at the K.I. Skryabin Moscow State Academy of Veterinary Medicine and Biotechnology (November 25, 2025).

Publications.

The research findings have been published in 15 scientific publications, including five articles in journals recommended by the Committee for Quality Assurance in Science and Higher Education of the Ministry of Science and Higher Education of the Republic of Kazakhstan, including the *Science and Education* journal of Zhangir Khan West Kazakhstan Agrarian-Technical University. One article was published in a journal indexed in the Scopus. In addition, six papers were presented and published in the proceedings of international scientific and practical conferences. The research also resulted in one utility model patent issued by the National Institute of Intellectual Property of the Republic of Kazakhstan and one recommendation for industrial implementation.

Structure and Scope of the Dissertation.

The dissertation comprises 153 pages, including appendices, with 138 pages of the main text. It consists of an introduction, a literature review, materials and methods, research results, discussion of the findings, conclusions, practical recommendations, and appendices. The dissertation is illustrated with 25 tables and 36 figures. The reference list includes 203 sources published in domestic and international scientific literature.

