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RESEARCH ARTICLE

Evaluation of protective properties of plants in the phytobiopreparation for the production of environmentally friendly cow's milk and improving the health of animals against the background of chronic intoxication with toxic metals Cd and Pb

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Abstract

The ecological problem of pollution of the environment and its components of water, soil, plants with toxic metals cadmium and lead has been exacerbated in various countries around the world, including and in Ukraine. In such conditions, the production of environmentally friendly cow's milk with pollutant content within domestic and international safety and quality standards becomes important. The purpose of research is to test and evaluate the protective properties of specially selected medicinal plants in the phytopreparation "BP-9" and the effectiveness of the synergistic effect of the complex application of the developed antidote substances (premix "MP-A" + phytopreparation "BP-9") on the concentration of cadmium and lead in milk, blood, kidneys and liver. Scientific and economic experiments were conducted on dairy cows with a live weight of 500 kg-545 kg. The first control group cows were fed the main diet without the addition of antidote premix "MP-A" and without injection of phyto-biological product "BP-9" developed from an aqueous extract of 9 medicinal plants. Animals of the second experimental group were introduced into the main diet as an antidote, a specially developed mineral-vitamin premix "MP-A", and in the third-fed premix and subcutaneous injection of plant phytopreparation "BP-9". In animals of the first control groups, the absorption of toxic metals cadmium and lead in the gastrointestinal tract gradually increased (accumulation), as indicated by their content in the blood, milk, liver and kidney. In cows of the second experimental group due to feeding the premix managed to achieve a stable decrease in the concentration of Cd and Pb, but much better antidote properties of the premix were manifested in synergy with the herbal preparation in the third experimental group. The high biological activity of the preparation is due to medicinal plants successfully selected for phytomorphological and biochemical properties. At this stage of research, it is difficult to assess the best and worst contribution to the experimental result of each of the plants, but in the complex their protective function worked by ensuring a satisfactory state of health of productive animals. In the third experimental group of cows, the content of toxic metals in milk after 120 days of the experiment decreased, the milk met the content of Cd and Pb to the requirements of environmental safety of the national standard and Regulations (EU) No853/2004 and No1881/2006) of the European Union.

Keywords: Medicinal plants, phytobiopreparation, extract, toxic metals, premix, milk, injection

Introduction

Heavy metals naturally exist in the environment, a significant amount of them enters the environment because of human activities, leads to pollution of air, soil, water resources, and they have caused one of the main global problems. These chemical elements are equally toxic to both plants and animals. After entering the body, most of them accumulate over a long period, causing various complications, for example, in plants, they can damage organs such as roots, leaves and cell components, or even interfere with such important biochemical processes as photosynthesis, absorption of mineral elements. In animals, they can also damage the main organs of the body, such as the kidneys, liver, and also cause serious diseases such as cancer. The disturbances caused by these heavy metals are highly dependent on their dose, exposure time and concentration. The toxicity of heavy metals has become a serious problem due to their hazardous nature, bioaccumulation and the like. Living things are influenced by these heavy

metals from various sources. They can enter the body with drinking water and food. Scientists have carried out important work to remove these metals from water using special adsorbents-magnetic nanoparticles of iron oxide; it is environmentally friendly, easy to use, and has good economic efficiency (Ata Ur Rehman et al. 2021). Reducing the flow of heavy metals from soil to plants-animal feed is also a challenge scientists are working on. Recent studies have shown that it is very difficult to remove heavy metals and radionuclides from the soil, but they can be effectively neutralized or converted into less toxic metabolites. In particular, the combination of a unique plant-microorganism system plays a key role in the recovery process. Currently, new methods of soil bioremediation are used to eliminate pollution with heavy metals and radionuclides. Microorganisms are capable of biotransformation, biosorption and biomineralization of these pollutants using their inherent catabolic process. Enhancing phytoremediation using a variety of strategies to ensure that land is safe, fertile and productive for sustainable use is certainly important for the livestock industry (Mayur Thakare, et al. 2021). The situation is more complicated when agricultural enterprises have already procured vegetable feeds that have an increased content of heavy metals, especially such dangerous ones as cadmium and lead, and these feeds are fed as part of the diet to productive animals-dairy cows. Unfortunately, anthropogenic pressure on agroecosystems is only increasing, which leads to their degradation (Blancard & Martin 2014; Gnatiuk 2018).

The release of cadmium and lead into the environment is associated with environmental risk to the body through cumulative toxicity and negative effects on internal organs and systems (Canty et al. 2014; Hashemi 2018; Roggeman et al. 2014). In animals, the intensity of growth and productivity decreases. The accumulation of the aforementioned heavy metals in environmental components and agroecosystems increases the risk of their intake into the body of cows and thereby poses a threat to human and animal health (Fischer et al. 2011; Rezza et al. 2018; Rahimi 2013). In chronic cadmium intoxication (nephrotoxicity, hepatotoxicity, immunotoxicity, osteotoxicity), oxidative stress of liver and kidney cells occurs, their damage and DNA damage, which can lead to carcinogenesis and oncological diseases (Liu et al. 2009).

Today, scientists are developing a large number of different methods, not only for the removal of toxic metals from the body of animals or humans but also protectors (antidote substances), which enhance the elimination of pollutants from the body. The corresponding antitoxic effect of enterosorbents and preparations is checked during scientific research.

The research aims to assess the protective properties of medicinal plants selected for the production of biologically active preparation "BP-9" in combination with the mineral and vitamin Premix "MP-A" according to the main criteria-the production of milk with the content of toxic metals within the permissible environmental safety standards and the back of dairy cows in terms of the content of pollutants in the blood.

Materials and Methods

To test the antidote properties of a biological product of plant origin, scientific and economic experiments were carried out in agro-ecosystems that are experiencing increased anthropogenic pressure around an industrial city. Scientific experiments were carried out on dairy cows of Ukrainian black and red-and-white dairy breeds. In the experimental farms, 126 cows were selected with the silage-haylage-concentrate type of feeding, 63 from the silage-haylage type, 36-from the silage-root and 195 from the silage-hay type of feeding, respectively. Animals selected by the analogs method were divided into three groups: the first control and the second and third research groups. The ratio of cows of all groups contained feeds with an increased concentration of heavy metals, especially such dangerous pollutants as cadmium and lead. A specially developed antitoxic mineral-vitamin premix "MP-A" was included in the diet of cows of the second research group, and the third-a premix+subcutaneous injection of a biological product "BP-9" made from an extract of 9 medicinal plants.

The biologically active preparation "BP-9", as well as the mineral and vitamin premix, was developed according to the methodology (Portjannyk 2002). 100 ml of the phytopreparation contains: *Schisandra chinensis*–15 ml, chamomile (pharmacy, peeled) (English Chamomile)–3 ml, *Eleutherococcus senticosus*–15 ml, medicinal sage (pharmacy) (English *Salvia officinalis)* –17 ml, common barberry (English Berberis)–12 ml, alfalfa –5 ml, kidney tea (English *Orthosiphon stamineus*)–15 ml, sea buckthorn (English Hippophae) rhamnoides)–15 ml, *Verbena officinalis*–3 ml. The dose of the herbal preparation "BP-9" is 20 ml/day, with the division of this norm into two, 10 ml each in the morning and at intervals of 12 hours in the evening. The frequency of administration of the preparation is 5 times a month, with an interval of administration once every 6 days. The preparation for injection was used for 42 cows of the third research group according to the silage-haylage-concentrate type of feeding 16.8 liters (20 ml × 20 (5 times

a month × for 4 months of the experiment)= 400 ml) silage-haylage-21 cows-8.4 liters, silage-root–12 heads–4.8 liters, silage-hay–65 heads-26 liters, respectively. A total of 56 liters of the preparation were manufactured and used. Release form–glass bottles with a volume of 250 ml. The biological product was manufactured under sterile conditions in a production laboratory according to the method (Hmel'nic'kij et al. 1994; Sokolov et al. 2002).

Feeding the premix based on the introduction of 1% into the diet (Podobed et al. 1996) was: for cows with a silage-root and silage-hay type of feeding 250 g per head per day, silage-haylage-concentrate-290 g, silage-haylage–255 g, respectively. Premix "MP-A" was fed for 24 heads of dairy cows of the second and third experimental groups with a silage-root type of feeding 720 kg (250 g per head per day × 24 heads × 120 days of experience) silage-hay–130 heads–3900 kg; silage-haylage–42 heads–1285.2 kg silage-haylage-concentrate–84 heads–2923.2 kg respectively.

The recipe (formula) of the "MP-A" premix and the herbal biological product "BP-9", the methodology for the development of the mineral and vitamin premix "MP-A" adapted to the fact of political daily rations belongs to the authors of this publication O. Mamenko and S. Portyannik (Ukraine).

The live weight of the cows selected for the experiment averaged 500 kg-545 kg, the average daily milk productivity 14.0 kg-14.8 kg, per lactation an average of 4270 kg-4514 kg of milk. The duration of the comparative period was 42 days, and the study period was 120 days. The cows selected by the method of analogs in terms of live weight, productivity were in the same conditions of feeding and keeping.

Laboratory analysis of samples of plant and animal origin: feed, blood, internal organs and tissues, urine and milk for the content of macro-, microelements, incl. heavy metals etc. were carried out by the method of atomic absorption spectrophotometry (spectrophotometer AAS-30) (Praice 1972). The results obtained were compared with physiological norms for blood (Skukovsky 1987), the content of heavy metals in internal organs with the maximum permissible concentrations specified in the mandatory minimum list of studies of raw materials, products of animal and plant origin, compound feed raw materials, compound feed, vitamin preparations, etc. which should be carried out in state laboratories of veterinary medicine and, based on the results of which a veterinary certificate (F-2) is issued, which are approved by the State Department of Veterinary Medicine environmental safety of milk was carried out per DSTU 3662-97 (Mamenko et al. 1997), as well as taking into account the requirements of international quality standards (Regulation (EU) No. 853/2004 and No. 1881/2006).

All manipulations with animals were carried out per the European Convention for the Protection of Vertebrate Animals used for Experimental and Scientific Purposes (Strasbourg 1986).

The data analysis was performed taking into account the peculiarities of the results obtained in the study: the sample size and type of data distribution, the nature of variances. For each sample, the mean value of the characteristic in the sample (M) and the Standard Deviation (SD) were calculated, the estimate is given as M ± SD. Disagreements between mean values were considered statistically probable at $P < 0.05$. The calculation was carried out in the STATISTICA software package version 10.0 for the Windows 7 operating system.

Results

Concentration of toxic metals in plants (Feed)

Under certain conditions, heavy metals that pollute the environment accumulate in the soil and easily migrate into plants. In plants that were used in the diet of dairy cows, an excess of the maximum permissible concentration of toxic metals was revealed.

Concentration of lead in the diet of cows with silage-root feeding type of feeding was 28.59 mg/kg in grass-legume hay (5.7 times excess), wheat straw 13.62 (2.7 times), corn silage 13.51 (2.7 times), Lucerne hay 16.78 (3.4 times), fodder beets 12.22 (2.4 times), corn puff 20.51 (4.1 times), respectively, cadmium-0.96 mg/ kg (3.2 times excess), 0.71 (2.4), 0.69 (2.3), 0.75 (2.5), 0.64 (2.1), 0.96 (3.2) respectively.

Concentration of lead in the diet of cows with silage-hay type of feeding was 11.22 mg/kg in alfalfa hay (2.2 times excess), wheat straw 12.5 (2.5 times), corn silage 9.13 (1.8 times), alfalfa haylage 9.54 (1.9 times), fodder beet 17.21 (3.4 times), barley mart 11.6 (2.3 times), respectively, cadmium-0.57 mg/kg (1.9 times excess), 0.51 (1.7), 0.39 (1.3), 0.45 (1.5), 0.75 (2.5), 0.54 (1.8) respectively.

Concentration of lead in the diet of cows with the silage-hay type of feeding was 16.51 mg/kg in alfalfa hay (3.3 times excess), cereal-legume hay 18.5 (3.7 times), corn silage 12.5 (2.5 times), alfalfa haylage 15.5 (3.1 times), roll with oatmeal 23.12 (4.6 times), roll with pea 23.51 (4.7 times), respectively, cadmium– 0.63 mg/kg (2.1 times excess), 0.66 (2.2), 0.48 (1.6), 0.54 (1.8), 0.75 (2.5), 0.78 (2.6) respectively.

Concentration of lead in the diet of cows with silage-

haylage-concentrate feeding was 16.52 mg/kg in alfalfa hay (3.3 times excess), cereal-legume hay 36.51 (7.3 times), corn silage 10.54 (2.1 times), alfalfa haylage 14.23 (2.8 times), pull corn 18.51 (3.7 times), pull pea 20.53 (4.1 times), respectively, cadmium–0.69 mg/kg (2.3 times excess), 0.75 (2.5), 0.42 (1.4), 0.48 (1.6), 0.54 (1.8), 0.63 (2.1), respectively.

Fluctuations in the content of hazardous pollutants in plants (feed) are due to different distances to the industrial center, prevailing winds, different amounts of agrochemicals used and the remoteness of agricultural land from highways, natural gas production facilities, a powerful gas compressor station, etc.

Plants to a greater extent accumulate heavy metals in the root system, that is, in the part that is in the soil, slightly fewer heavy metals enter the vegetative system, therefore, of all feeds, fodder beets had the highest level of contamination for all studied elements in comparison with others feed. In fodder grown on agricultural machinery, where the cows are fed a silage-haylage-type diet, in addition to exceeding the maximum permissible concentrations for the content of Cd, Pb, Cu, Zn, in comparison with other experiments, high content of zinc in oats and peas was recorded on average. 6.3-6.8 times. Pea bran had the highest content of cadmium and lead among other feeds, and cereal-legume hay was distinguished by the highest content of copper (3.9 times). The feed ration of cows with the silage-haylage-concentrate type of feeding had the highest contamination in terms of lead by 7.3 times, zinc by 7.8 times and copper by 4.1 times. In terms of feed contamination with cadmium, these ration ranks last along with the ration where the animals were fed by silage-haylage type of feeding. The highest content of cadmium, lead and copper among the ration feed was distinguished by cereal-legume hay, and the total zinc accumulated in the grain of maize. According to the level of feed contamination, the ration type of feeding can be placed as shown in Fig. 1.

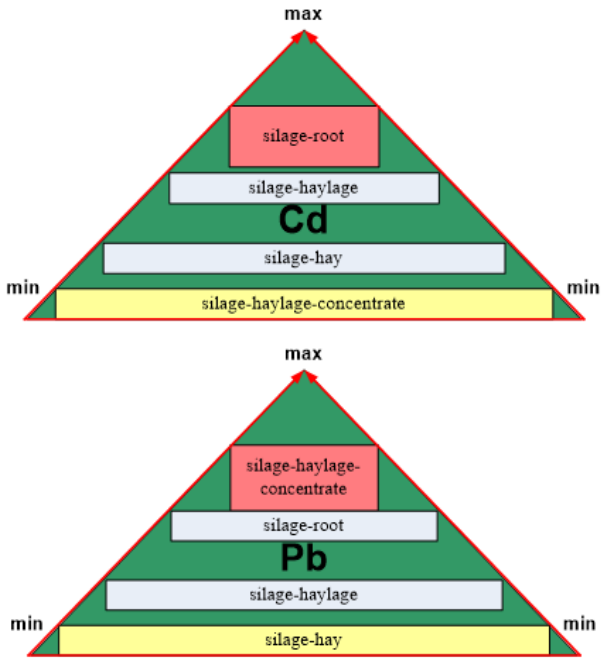

Figure 1. Location of the types of cows feeding according to the level of feed contamination with toxic metals Cd and Pb silage-haylage-concentrate feeding, respectively 1 nmol/l-77.94 nmol/l ± 0.99 nmol/l, 2-40.64 ± 0.54 (p<0.01) and 3 nmol/l-32.14 nmol/l ± 0.55 nmol/l (p<0.01) (Cd) and 1 nmol/l-4.63 nmol/l ± 0.37 µmol/l, 2-1.72 ± 0.17 (P <0.01), 3-1.27 ± 0.22 (P <0.01) (Pb) in accordance with the physiological norm of cadmium in the blood at the level of 20 nmol/l-50 nmol/l, and lead up to 2 µmol/l. The sample of animals is the same-5. All comparisons of the obtained blood test results in 2 and 3 experimental groups with 1 control group.

Analysis of blood for the content of toxic metals

Analysis of the blood of experimental animals showed that heavy metals from the gastrointestinal tract were absorbed into the blood. The cadmium content in the blood of cows of the 1st control group with silage-root feeding type was 98.34 nmol/l ± 1.03 nmol/l. The use of a special antitoxic mineral and vitamin premix "MP-A" in the feeding of cows in the 2nd experimental group blocked the absorption of the element and its level was 79.11 ± 2.90 at p<0.01 compared with the control group (n=5). Intradermal injection of the herbal preparation in experimental group 3 with simultaneous feeding of the MP-A premix (complex effect) enhanced the antidote protective effect, proves the cadmium content in the blood at the level of 49.19 ± 2.41 (p<0.01). A similar situation was observed for lead 8.32 µmol/l ± 1.65 µmol/l, 3.02 ± 0.99 (p<0.01) and 1.98 ± 0.16, respectively, for p<0.01 in comparison with the control group (n=5). The same results, in terms of the content of cadmium and lead in the blood, against the background of chronic intoxication of the body of dairy cows with heavy metals and the use of a premix and herbal biological product, were obtained in experiments with other types of animal feeding. Thus, the cadmium content in the blood of cows of the 1st control group with the silage-hay type of feeding was 101.20 nmol/l ± 3.17 nmol/l, 2-54.29 ± 2.64 (p<0.01) and 3 nmol/l-40.72 nmol/l ± 1.98 nmol/l (p<0.01), respectively, and lead 6.54 µmol/l ± 0.45 µmol/l, 4.01 ± 0.64 (p<0.01), 1.38 ± 0.28 (p<0.01), respectively; silage-haylage the concentration of Cd in the blood of animals of the 1st control group was 81.17 nmol/l ± 0.60 nmol/l, 2–48.19 ± 0.73 (p<0.01) and 3–41.61 ± 1.05 (p<0.01), respectively, the concentration of Pb in the blood was 5.74 µmol/l ± 0.32 µmol/l, 2.07 ± 0.16 (p<0.01), 1.87 ± 0.09 (p<0.01), respectively.

Thus, the content of toxic metals cadmium and lead in the blood of cows of only the third research group, where the herbal preparation was injected with subcutaneous injection, was within the physiological norm, regardless of the type of feeding. In the second group, where the premix itself was developed (without injection of the

phytopreparation "BP-9"), the content of cadmium and lead was within the physiological norm only in animals whose diet was a silage-haylage-concentrate type of feeding. Therefore, the positive antitoxic, protective effect of the biological product and its plant components is obvious. A constant examination of the state of health of the experimental animals by a veterinarian also confirms this.

Content of toxic metals in milk

In the course of an experiment to test the antidote properties of herbal biological products, it is important to assess its effect on the safety of milk produced. Without the use of protectors with blood flow, toxic metals freely enter the mammary gland, then into milk. Chemical analysis of selected milk samples, according to a random sample of animals n=5, showed higher levels of cadmium in the milk of animals of control groups 1 with different types of feeding and, accordingly, amounted to 0.087 mg/kg ± 0.008 mg/kg (silage-root type of feeding), 0.09 ± 0.085 (silage-hay), 0.068 ± 0.017 (silage-haylage) and 0.053 ± 0.019 (silage-haylage-concentrate) at a rate of 0.03 mg/kg. Likewise, in terms of lead content 1.835 mg/kg ± 0.093 mg/kg (silage-root), 1.641 ± 0.253 (silage-hay), 1.734 ± 0.148 (silage-haylage) and 1.794 ± 0.165 (silage-haylage-concentrate) at a rate of 0.02 mg/kg. Injection of the herbal preparation "BP-9" in 3 experimental groups of dairy cows in addition to feeding the premix "MP-A" contributed to the strengthening of the protective function of the body, manifested itself in a decrease in the concentration of toxic metals not only in the blood of animals of these groups but also in milk. At the same time, only milk of cows from 3 research groups from silage-root 0.018 mg/kg ± 0.002 mg/kg (Cd), 0.014 ± 0.003 (Pb) and silage-haylage 0.012 mg/kg ± 0.002 mg/kg (Cd), 0.014 mg/kg ± 0.004 mg/kg (Pb) the type of animal feeding corresponded to domestic and international environmental safety standards. The degree of reliability in comparison with the data of the control group is $p<0.01$.

Statistical analysis

To establish the correspondence of the obtained data to the law of "normal" distribution (Gaussian), let's apply the Shapiro-Wilk W test, which is considered the most powerful, especially in small samples ($n<50$) of independent groups. The cadmium content in the blood and milk of cows does not obey the law of normal distribution. The Shapiro-Wilk test made it possible to determine the appropriate method for further analysis of the comparison of samples. Considering that the sample size is insignificant, the most effective way to use the nonparametric analysis of variance Kruskal-Wallis (or H-test) (Kruskal-Wallis ANOVA) (Fig. 2). Fig. 3 and Fig. 4 show descriptive statistics indicators.

The obtained results of laboratory analyzes do not obey the law of normal distribution, therefore, let's consider it necessary to bring into the arithmetic mean values of the studied indicators by groups, as well as the median from the lower and upper quartiles (Figs. 5 and 6). A small

a

Kruskal-Wallis ANOVA by Ranks; Cd (Spreadsheet1)
Independent (grouping) variable: Group
Kruskal-Wallis test: H (2, N= 15) =12,50000 p =,0019

Depend.: Cd	Code	Valid N	Sum of Ranks	Mean Rank
1	1	5	65,00000	13,00000
2	2	5	40,00000	8,00000
3	3	5	15,00000	3,00000

b

Kruskal-Wallis ANOVA by Ranks; Cd (Spreadsheet1)
Independent (grouping) variable: Group
Kruskal-Wallis test: H (2, N= 15) =12,50000 p =,0019

Depend.: Cd	Code	Valid N	Sum of Ranks	Mean Rank
1	1	5	65,00000	13,00000
2	2	5	40,00000	8,00000
3	3	5	15,00000	3,00000

Figure 2. The value of the error p is given for the null hypothesis that the Cd content in the blood and milk of cows in different experimental groups does not differ, in our case $p<0.05$ the studied groups are statistically significantly different from each other.

Descriptive Statistics (Spreadsheet1)

Variable	Valid N	% Valid obs.	Mean	Median	Sum	Minimum	Maximum	Lower Quartile	Upper Quartile	Std.Dev.	Standard Error
1 Group	5	33,33333	98,34400	98,76000	491,7200	96,89000	99,51000	97,74000	98,82000	1,029335	0,460332

Descriptive Statistics (Spreadsheet1)

Variable	Valid N	% Valid obs.	Mean	Median	Sum	Minimum	Maximum	Lower Quartile	Upper Quartile	Std.Dev.	Standard Error
2 Group	5	33,33333	79,11200	78,71000	395,5600	75,91000	83,62000	77,52000	79,80000	2,904491	1,298928

Descriptive Statistics (Spreadsheet1)

Variable	Valid N	% Valid obs.	Mean	Median	Sum	Minimum	Maximum	Lower Quartile	Upper Quartile	Std.Dev.	Standard Error
3 Group	5	33,33333	49,19000	49,26000	245,9500	45,74000	52,01000	48,21000	50,73000	2,407893	1,076843

Figure 3. Descriptive statistics of the studied indicators: arithmetic mean M (Mean), Standard Deviation SD (Std. Dev.), median (Median), lower and upper quartiles (Lower Quartile; Upper Quartile) and other Cd contents in the blood of cows of three experimental groups with silage-root feeding type.

a

Variable	Descriptive Statistics (Spreadsheet1)								
	Valid N	% Valid obs.	Mean	Median	Sum	Minimum	Maximum	Std.Dev.	Standard Error
Group 1	5	33,33333	0,086600	0,087000	0,433000	0,076000	0,096000	0,008264	0,003696

Variable	Descriptive Statistics (Spreadsheet1)								
	Valid N	% Valid obs.	Mean	Median	Sum	Minimum	Maximum	Std.Dev.	Standard Error
Group 2	5	33,33333	0,031400	0,031000	0,157000	0,025000	0,040000	0,005683	0,002542

Variable	Descriptive Statistics (Spreadsheet1)								
	Valid N	% Valid obs.	Mean	Median	Sum	Minimum	Maximum	Std.Dev.	Standard Error
Group 3	5	33,33333	0,018400	0,019000	0,092000	0,015000	0,021000	0,002408	0,001077

b

Variable	Descriptive Statistics (Spreadsheet1)								
	Valid N	% Valid obs.	Mean	Median	Sum	Minimum	Maximum	Std.Dev.	Standard Error
Group 1	5	33,33333	1,835400	1,836000	9,177000	1,734000	1,976000	0,093042	0,041610

Variable	Descriptive Statistics (Spreadsheet1)								
	Valid N	% Valid obs.	Mean	Median	Sum	Minimum	Maximum	Std.Dev.	Standard Error
Group 2	5	33,33333	0,614200	0,598000	3,071000	0,538000	0,757000	0,085268	0,038133

Variable	Descriptive Statistics (Spreadsheet1)								
	Valid N	% Valid obs.	Mean	Median	Sum	Minimum	Maximum	Std.Dev.	Standard Error
Group 3	5	33,33333	0,014400	0,014000	0,072000	0,011000	0,019000	0,003209	0,001435

Figure 4. Descriptive statistics of the studied indicators: arithmetic mean M (Mean), Standard Deviation SD (Std. Dev.), Median (Median), lower and upper quartiles (Lower Quartile; Upper Quartile) and other contents of Cd (a) and Pb (b) in the milk of three cows test groups with silage-root feeding type.

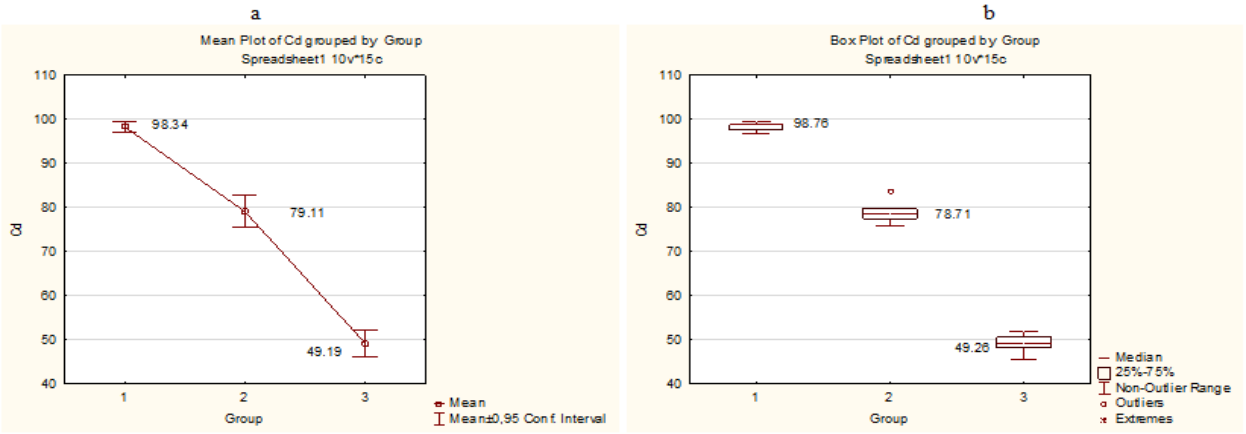

Figure 5. Diagram of (a) mean values and (b) quartile diagram of Cd content in blood (nmol/l) of cows of three experimental groups with silage-root type of feeding.

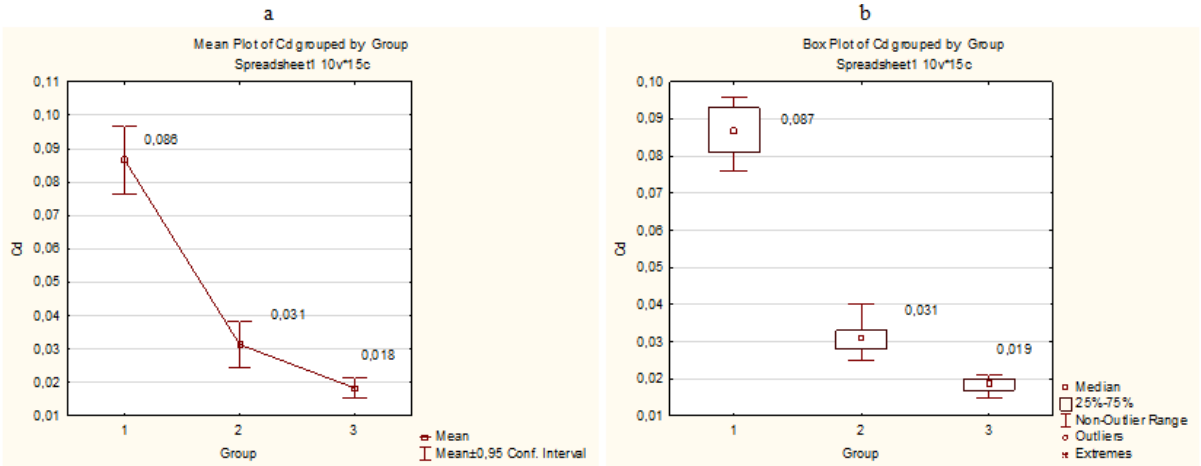

Figure 6. Diagram of (a) mean values and (b) quartile diagram of Cd content in milk (mg/kg) of cows of three experimental groups with silage-root feeding type.

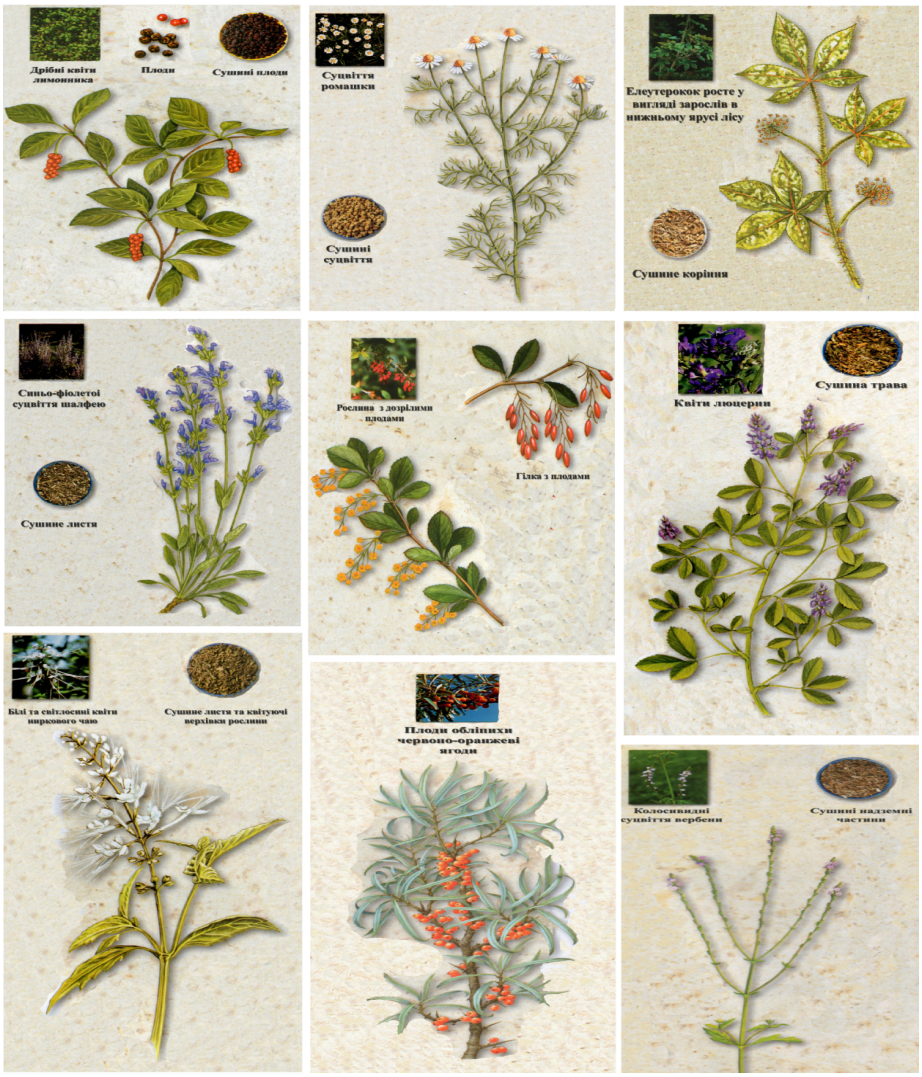

Figure 7. *Schizandra chinensis,* medicinal chamomile (pharmacy, peeled) (chamomila recutita), *Spiny eleutherococcus (Eleutherococcus senticosus (Acanthopanax senticosus)), Salvia officinalis* (pharmacy) (*Salvia officinalis*), common barberry (*Berberis vulgaris*), alfalfa (*Medicago sativa*), kidney tea (*Orthosiphon stamineus*), sea buckthorn (*Nyppophae rhamnoides*), medicinal verbena (*Verbena officinalis*) and their formulations for the manufacture of the biological product "BP-9".

difference between the average values of the indicators and their median is insignificant and in this experiment, there is no significant effect on the research results.

Characteristics of herbal preparation

Analysis of the data obtained indicates that the toxic effect of lead and especially cadmium on the body of dairy cows is difficult to reduce without the use of additional techniques. The premix and phytopreparation "BP-9" developed and applied by us in a complex scientific experiment as a whole gave a good result, acting as protectors (antidotes). At the same time, a significant role belongs not only to the mineral elements and vitamins introduced into the "MP-A" premix, but also to the successfully selected medicinal plants from which the extract was made, and then the phytobiopreparation "BP-9" itself (Fig. 7).

Concentration of Cd and Pb in internal organs

Tab. 1 shows the chemical composition of the preparation with the content of mineral elements and vitamins.

Due to the intake of heavy metals into the body of cows with plant feed, not only does their content in the blood and milk of animals of the first control groups but also has a manifestation of accumulation in the internal organs. It should be noted that the elimination of heavy metals from the body with urine is negligible. The likelihood of an increase in the excretion of all heavy metals studied by us in the urine without the use of additional funds is unlikely. Therefore, pollutants, which are found in the body of cows, accumulate in various organs and tissues, in particular, liver, kidneys, as organs "targets" (Tab. 2), are excreted with the secretion of the mammary gland.

Table 1. "BP-9" chemical composition.

No.	Substance	Contained in 100 ml
	Macro-elements, Micro-elements	
1	Iron, mg	9.64
2	Selenium, mg	45.22
3	Molybdenum, mg	36.41
4	Boron, mg	3.2
5	Calcium, mg	47.81
6	Chromium, mg	4.8
7	Fluorine, mg	15.36
8	Sodium, mg	10.11
9	Lithium, mg	6.9
10	Iodine, mg	31.94
11	Silicon, mg	19.72
12	Manganese, mg	34.56
13	Copper, mg	2.69
14	Zinc, mg	6.8
15	Nickel, mg	18.7
16	Vanadium, mg	6.3
17	Bromine, mg	8.6
18	Cobalt, mg	53.19
	Vitamins	
19	A (retinol acetate), g	1.04
20	C (ascorbic acid), mg	72.96
21	E (alpha-tocopherol acetate), g	0.18
22	B1 (thiamine), mg	25.7
23	B2 (riboflavin), mg	18.56
24	B3 (niacinamide), mg	54.23
25	B4 (choline chloride), g	10
26	B5 (PP) (niacin), mg	250
27	B6 (pyridoxine), mg	34.6
28	B12 (cyanocobalamin), mcg	4.5
29	B12 (cyanocobalamin), μg	4.5
30	K, g	2.21
31	F, mg	37.04

Taking into account the maximum permissible concentration of cadmium and lead, according to the mandatory minimum list of studies of raw materials, products of animal and plant origin, compound feeds raw materials, compound feed, vitamin preparations, etc. established for kidneys at the level of 1.0 mg/kg (Cd and Pb), liver 0.3 mg/kg (Cd), and 0.6 mg/kg (Pb) in animals of the first control groups, where antidote substances were used, the concentration of toxic metals gradually increased, as evidenced by the results of control slaughter of animals and laboratory studies of internal organs (Tab. 2). In the second and third research groups, with the help of the developed protectors and especially the herbal preparation, it was possible to delay the flow of pollutants to the data of the internal organs and to enhance their elimination from the body with excrement into animals with various types of feeding. Only in cows of the second experimental group according to the silage-root type of feeding, where the premix itself, the cadmium content slightly exceeded the permissible norm and amounted to 1.294 mg/kg ± 0.017 mg/kg, but the tendency for a decrease in accumulation is very likely at $p<0.01$ compared to the 1st control group. A similar situation was recorded for the content of lead but in the liver 1.383 mg/kg ± 0.032 mg/kg ($p<0.01$). If the plant biological product and its biologically active substances, on the contrary, increased the flow of pollutants to the internal organs, obviously we would observe degenerative changes in these organs, due to disruption of the nephrons, coiled tubules, hepatocytes, etc. incl. specific diseases, for example, proteinuria, which we did not observe. In the course of the experiment, all the animals set for the experiment were constantly under the supervision of a veterinarian and no such diseases were found in cows.

Table 2. The content of toxic metals in the internal organs of cows at the end of the experimental period (M ± SD).

Feeding type	Mineral elements	Cow group		
		1 control	2 experimental	3 experimental
		Kidney		
Silage-root	Cadmium, mg/kg	3.241 ± 0.029	1.294 ± 0.017	0.903 ± 0.016
	Lead, mg/kg	4.522 ± 0.044	0.931 ± 0,079	0.851 ± 0.051
Silage-hay	Cadmium, mg/kg	2.968 ± 0.017	0.884 ± 0.021	0.701 ± 0.019
	Lead, mg/kg	4.387 ± 0.031	0.804 ± 0.042	0.735 ± 0.038
Silage-haylage	Cadmium, mg/kg	2.634 ± 0.023	0.831 ± 0.017	0.695 ± 0.012
	Lead, mg/kg	3.981 ± 0.030	0,772 ± 0.061	0.639 ± 0.028
Silage-haylage-concentrate	Cadmium, mg/kg	2.305 ± 0.027	0.721 ± 0.021	0.563 ± 0.025
	Lead, mg/kg	3.452 ± 0.049	0.785 ± 0.024	0.721 ± 0.017
		Liver		
Silage-root	Cadmium, mg/kg	0.752 ± 0.029	0.283 ± 0.011	0.271 ± 0.022
	Lead, mg/kg	1.865 ± 0.030	1.383 ± 0.032	0.589 ± 0.014
Silage-hay	Cadmium, mg/kg	0.701 ± 0.019	0.368 ± 0.030	0.255 ± 0.026
	Lead, mg/kg	1.731 ± 0.029	0.557 ± 0.047	0.505 ± 0.035
Silage-haylage	Cadmium, mg/kg	0.683 ± 0.046	0.247 ± 0.019	0.234 ± 0.033
	Lead, mg/kg	1.694 ± 0.017	0.489 ± 0.057	0.463 ± 0.023
Silage-haylage-concentrate	Cadmium, mg/kg	0.611 ± 0.037	0.239 ± 0.041	0.205 ± 0.038
	Lead, mg/kg	1.607 ± 0.022	0.440 ± 0.036	0.415 ± 0.030

Note: the degree of reliability in comparison with the data of the control group is $p<0.01$; n=3.

Thus, an analysis of blood, milk and the results of an acute experiment indicate a slow chronic intoxication with toxic metals. Against this background, the antidote premix "MP-A" contributed to a decrease in the absorption of these toxicants in the gastrointestinal tract, and the plant biological product "BP-9" acted as bio-protectors, protecting internal organs from toxic shock. The complex application of such a technique in animal feeding and the injection of a phytopreparation ensured the production of ecologically safe cow's milk–the dynamics of a decrease in the cadmium content in the milk of cows with silage-haylage-concentrate feeding 0.053 mg/kg ± 0.019 mg/kg in the control group, 0.024 ± 0.009 in the second experimental group, and 0.014 mg/kg ± 0.004 mg/kg in the third experimental group, lead 1.794 mg/kg ± 0.165 mg/kg, 0.331 mg/kg ± 0.064 mg/kg and 0.032 mg/kg ± 0.008 mg/kg, respectively ($p<0.01$). At the same time, the maximum permissible concentration of cadmium content according to the DSTU 3662-97 standard is set at 0.03 mg/kg, lead 0.1 mg/kg, and Regulation (EU) No. 1881/2006 at 0.02 mg/kg, copper-0.26-0.35 and zinc-3-5 mg/kg, respectively. At the same time, the experimental cows as a whole had a satisfactory state of health, and the protective effect of the antidote substances we have developed, and especially the herbal preparation, can be assessed as successful.

Discussion

Nature is a source of active substances of plant origin. The healing resources of the plant kingdom have not been fully studied, systematic research aimed at creating new medicinal products from plant materials is being intensively carried out all over the world. The flora of our planet has hundreds of plant species, of which about 250,000 have been described to date, and only 2-3 thousand species have become objects of pharmacological and chemical research. Some of these studies were carried out quite a long time ago and today they need to be repeated taking into account the current ecological state and the development of science. Our research is aimed at the selection of appropriate types of medicinal plants, the healing properties of which are well known, but their influence on the removal of heavy metals of ecocide origin and support for the functioning of various organs and systems that experience the toxic impact of xenobiotics in the body of dairy cows, the production of ecologically safe milk, have been studied not enough.

It takes time to obtain an effective biologically active preparation. Once the samples are accurately identified and the plants are collected in sufficient quantities, it is up to chemists and scientists to extract extracts from them to isolate the chemical components of the plants in pure form or a mixture. We have selected plants with sufficiently studied medicinal properties and the content of the corresponding biologically active substances, which in the aggregate effect provided a protective result and an antitoxic effect. We tried to take into account the possibilities of veterinary medicine doctors and technologists of livestock production to identify (presence) appropriate plants, possibly on the territory of farms, or local ecosystems, but so that the plants do not end up in the Red Book, endemics, relicts, and the like. In the course of the experiment, the effectiveness of the phytobiological preparation BP-9 developed by us from the extract of medicinal plants was tested on experimental dairy cows. We got a positive result, which is manifested in the preservation of the health of productive animals and the production of environmentally friendly milk with cadmium and lead content within the permissible limits. Scientists (Hejna et al. 2018) indicate the danger of the heavy metals we study in animal feed, livestock products and, in general, in human nutrition. It is noted that such pollutants as cadmium and lead do not have established positive biological functions in the animal or human body, therefore, they are considered as pollutants, such that are not desirable in feed (Reg. 2002/32/EU), animal feeding, can lead to systemic violations at the cellular level (Tab. 3).

Table 3. Heavy metals according to (Theron, et al. 2012 and Govind & Madhuri 2014).

Essential elements (allowed in animal feeding) **	Unimportant elements (undesirable in animal feeding) ***
Co	As
Cr	Cd
Cu	Hg
Fe	Pb
Mn	
Mo	
Ni	
Se	
Zn	

*Additives permitted in animal feeding in accordance with regulation EU No. 1831/2003.
**Undesirable items according to directive 2002/32/EU.

We have succeeded in producing milk with cadmium and lead content within the permissible domestic and international safety standards.

About half of the medicines used in our time are created based on plant raw materials, and one quarter contains plant extracts or active substances obtained directly from plants. Plants are found in semi-synthetic and phytotherapeutic medicines and thus underlie the most common treatments. But the development of plant extracts for the removal of heavy metals such as

cadmium, lead, etc. and the restoration of homeostasis of intoxicated organisms has not been carried out, it has not been studied enough.

People have long used plants to fight various ailments. Even Hippocrates (460 BC-377BC), who is considered the father of medicine, recommended asparagus and garlic as a diuretic, like a poppy for sleeping pills, and willow leaves to reduce pain and reduce fever. Dioscorides created the first herbalist–a list of medicinal plants. The new era for medicinal plants, starting from the 30s of the twentieth century, reached such a development that it became possible to synthesize active substances similar to those found in plants. But medicine has not abandoned the use of plants. Today, there are two main areas of application of plants: the first is where only plants are used for treatment, and the second is where plants become material for the production of medicines.

Modern scientific research requires the discovery of new biologically active substances and preparations since a person remains defenseless and unarmed to various diseases and especially those caused by the deterioration of the ecological situation. Therefore, the continuous search for effective medicinal plants and the production on their basis of effective biologically active preparations such as the herbal preparation "BP-9" developed by us, incl. those that contribute to the elimination of heavy metals from the body are an urgent problem for scientists and practitioners. We have not only developed, but also researched a phytopreparation. We studied its pharmacodynamics (the proportion of the preparation from application to the conclusion, which depends on the established dose) and pharmacokinetics (the body's response to the preparation, the biological effect on the body from the use of the preparation).

The etiopathogenesis of body poisoning with cadmium and lead is complex. Inorganic compounds of cadmium and lead in the gastrointestinal tract react with acid to form more soluble salts, which bind to proteins to form albuminates. In the blood, the bulk of cadmium and lead penetrates erythrocytes, forming cadmium and lead lipoprotein complexes in the membranes. These elements reduce the resistance of erythrocytes, increase the permeability of the cell membranes, which results in the loss of potassium and water. Hemolysis of blood erythrocytes occurs, hemoglobin is destroyed with the accumulation of free bilirubin, which disrupts the phosphorylation processes in brain cells.

Cadmium and lead are typical communicative poisons that accumulate in the liver, kidneys, bones, spleen, and other organs (Tab. 2). Their soluble compounds in tissues block sulfhydryl groups of many enzymes, subsequently manifested by a violation of the structure and function of the nervous tissue, kidneys, liver, walls of blood vessels, the endocrine system, etc. Possible acute poisoning in which anxiety is manifested in animals, alternating with a depressed state, muscle tremors, convulsions, salivation, diarrhea, thirst, loss of appetite, etc., but today more and more chronic poisoning of animals and, in particular, dairy cows is observed, as it was established. It was registered with a simultaneous decrease in the quality of the produced product–milk. In chronic poisoning, the latency period can be long, even up to one year. In animals, general weakness is noticed, weight loss, loss of live weight, swelling of the joints, diarrhea, which are overwhelmed by constipation, anuria is possible. Convulsions develop, atrophy of the muscles of the back and pelvic limbs, the development of osteodystrophy, etc. What kind of pharmacological correction can be under the given conditions? In the overwhelming majority, it is recommended to flush the stomach with clean warm water or 1% bicarbonate solution. If a specialized enterprise has 100 dairy cows, such a procedure is extremely difficult to do, not to mention 200 or 600 heads, etc. As a weakening substance, magnesium sulfate or sodium sulfate is prescribed, which converts cadmium and lead compounds into insoluble salts, which are excreted from the body through the gastrointestinal tract. For faster removal of pollutants from tissues, complex ones such as calcium tetacin, unitiol, and the like are used. The use of vitamins C, B1, cyanocobalamin, cocarboxylase, diuretics, anticonvulsants, sedatives, anti-inflammatory and other preparations are shown. At the same time, we know the side and adverse effects of synthetic compounds such as magnesium sulfate, sodium sulfate, calcium tetacin, unitiol, etc. on the animal organism. Moreover, it is impossible to provide prophylaxis and a prolonged antidote therapeutic effect with these substances, not to mention the simultaneous production of ecologically safe high-quality milk.

We went the other way and as antidote substances that contributed to the simultaneous removal of heavy metals from the body of productive cows, restoring their homeostasis, preventing intoxication and poisoning, strengthening the immunity and general health of animals, improving their physiological state, etc. in large-scale farms, specializing in the production of cow's milk, they tested in scientific and economic experiments an extract from a corresponding set of medicinal plants, which, in our opinion, have corresponding biologically active substances that have replaced the already existing and well-studied synthetic compounds. At the same time,

preparation of the preparation is simple and affordable for specialists working with animals.

For the introduction of the biologically active preparation "BP-9" to plants of origin into the organism of experimental cows, we used its liquid dosage from an extract from 9 most important, in our opinion, medicinal herbs. The nature and strength of action of a medicinal substance completely depend on its chemical composition, and the effect on organs, tissues and interactions with other substances, incl. heavy metals Cd, Pb and their excretion from the body occurs at a certain concentration. The concentration depends on the intensity of absorption into the blood and lymph, its distribution in tissues, and biotransformation. The effectiveness of the antidote action of a phytopreparation depends not only on the administered dose of the preparation but also on the type of injection, the rate of absorption, which affects the penetration of the corresponding chemicals into the cells, which can form stable chelate complexes with heavy metals and ensure their elimination outside the body. In terms of intoxication with heavy metals, it is the cells of the liver, kidneys, spleen, muscle tissue, bones, and lungs that are most susceptible to the accumulation of contaminants. Therefore, it is in the cells of these organs that the medicinal substance should be directed to the phytobiopreparation.

When creating a phytobiopreparation, it is necessary to remember the duration of its action, which is determined by the intensity of the inactive and excretion from the body. Absorption, distribution, biotransformation and excretion of medicinal substances from the body occur in the process of penetration through cell membranes. Each cell has its membrane, mitochondria and nucleus. The mucous membrane of the gastrointestinal tract, the skin has layers of various cells, but despite the anatomical features, diffusion and transport of medicinal substances (ligand groups for the formation of chelates with heavy metals) from them occurs very similarly.

The cell membrane consists of a bimolecular lipid layer on both sides of the protein layer, between which there are pores filled with water. The thickness of the membrane of cells of various organs is 100 Å (angstroms), and the pores of various membranes range from 4 Å to 40 Å. The lipid membrane passes fat-soluble substances well and water pores-water-soluble substances. Therefore, the intensity of the transport of ligand groups and preparations will depend on physicochemical characteristics, such as the volume and shape of molecules, the degree of ionization and the fattiness of ionized and non-ionized forms. There are several mechanisms for transporting chemicals through biological membranes: passive diffusion along the concentration gradient, that is, towards a lower concentration; facilitated diffusion –filtration through the pores of membranes in the form of complex compounds with other structures; active diffusion–transport by carrier enzymes against a concentration gradient; pinocytosis–absorption of substances by the membrane with the formation of depressions, pinocytic vesicles and vacuoles.

The overwhelming majority of medicinal substances can penetrate cell membranes through passive transport or active special transport systems. Fat-soluble substances penetrate the membranes through passive diffusion. The intensity of transportation is directly proportional to the concentration of the substance in the membrane and the fat-water distribution coefficient. Non-polar and polar substances, poorly soluble in lipids, penetrate through water pores (filtration) due to the existence of a hydrostatic and osmotic difference on both sides of the membrane. That is why we decided to choose a liquid form of preparative use as an antidote to biologically active phytopreparation. For this, an infusion was prepared under sterile conditions-an aqueous extract-extract of medicinal substances from plant raw materials. We chose 9 medicinal plants, which are natural substances without admixtures of chemicals. In medicine, similar herbal biologically active preparations are used, containing many more or less environmentally friendly components of representatives of terrestrial and marine flora. The preparations are recommended to be used as strong bactericidal and anti-inflammatory agents for inflammatory processes in the intestines of young animals; as antidepressants and adaptogens-during severe stress in animals; as radioprotectors for animals in areas contaminated with radionuclides, etc. We used only 9 of the most necessary, in our opinion, components to remove heavy metals from the body of animals and enhance their protective functions.

We prepared the infusion according to the well-known method (Hmel'nic'kij et al. 1994; Sokolov et al. 2002) according to the following scheme: first, we grind the plants, then mix and prepare an extract of biologically active substances, for this weighed amount of dried plant parts, pour into a vessel previously heated for 15 minutes in a boiling water bath and fill it with distilled water at room temperature, close with a lid, put in a boiling water bath or infusion apparatus (for infusion for 15 minutes). Then refrigerate at room temperature for 45 minutes. We get a liquid called colatura or extract. Add the missing amount of infusion with boiled water by rinsing the squeezed weighed amount of dried plant parts. When making an extract with a volume of 1 liter-3 liters, heating

in a water bath for infusion was increased to 25 minutes. Filter the prepared solution under sterile conditions through cotton wool or cotton wool and gauze, filter through a double filter made of cotton wool and filter paper. Rinse the glass with the first part of the filtrate and pour it onto the filter of the funnel for re-filtration to remove the soft hair of cotton wool, etc. After the end of filtration, we check the solution for purity; if necessary, we carry out repeated filtration; we seal the glass with a cork and put it in a storage place protected from light at a temperature of 5°C-10°C.

The body of an animal consists of many substances, the main ones of which are: oxygen, calcium, sodium, chlorine, carbon, phosphorus, magnesium, fluorine, hydrogen, potassium, iron, silicon, nitrogen, sulfur, iodine, manganese, etc., in addition the entire process of cell regeneration of the body takes place directly in it. If the cells, tissues and blood, organs and glands, other parts of the body do not contain these elements in the required proportion, or if their balance is insufficient, plus the load of the body with such dangerous heavy metals as cadmium and lead they affect the decrease in the content of the above elements, acting as antagonists, thereby disrupting the balance of macro- and microelement nutrition, then, accordingly, the balance of the body's functions are disturbed, and a state of toxemia begins to manifest itself.

Natural plants in the process of the formation of organic matter (during photosynthesis) use all the macro- and micro-elements in the soil, therefore, all nine plant components contain a sufficiently large amount of the above and other mineral elements necessary for the body, which is sufficient for antidote protective action, especially in conditions of intoxication, as well as several other nutrients, vitamins (Tab. 1).

Schizandra chinensis

Its extract in the composition of the "BP-9" preparation influenced precisely the kidneys, liver and other organs of the "target", which experience the ecocidal effects of cadmium and lead. Contains citric, malic and tartaric acids, as well as schisandrin, sugar, tannides, vitamin E, up to 33.8% fatty oil from glycerides of linolenic and oleic acids. Among the mineral elements of the plant is iron, manganese, phosphorus, calcium. This medicinal plant is recommended as a hepatoprotector, since it reduces the intensity of hepatic lipid oxidation. By stimulating the activity of antioxidants, it affects the immune defense of the body. Protects cells and muscles. Experts point to a protective function against breast cancer, quite possibly in case of intoxication with cadmium and lead. Tones up the cardiovascular system of warm-blooded animals increase blood pressure and the amplitude of heart contractions stimulates breathing (the rhythm becomes more frequent and the amplitude of respiratory movements deepens). Recommended for the prevention of chronic infectious diseases and intoxication. Excites the central nervous system, causes neuromuscular excitability. In his experiments on rats (Eun Young Kim et al. 2011), he also indicates a cardioprotective effect, a decrease in cholinesterase activity, and a promising role of the extract in the prevention of cardiovascular diseases. In an experiment on sports horses, scientists (J. Hancke et al. 1996) note that after oral administration of a standardized dried extract of this plant for 14 days, the level of gamma-glutamyltransferase and glutamic oxacetic transaminase in blood serum significantly decreased, which made it possible to conclude that early recovery of sports horses during training. In general, the interaction of plant components with estrogen receptors, as well as their antioxidant and anti-enzymatic activity, is being actively studied today, a large number of other studies are being carried out, indicating increased interest, but in such experiments on dairy cows, the plant extract was not used. There is no information on the toxicity of the plant, so the introduction of the extract into the herbal preparation is safe.

Thus, in the course of the experiment, the plant extract performed well its function, as bio-protectors protecting liver and kidneys from the toxic load of cadmium and lead, prevented hepatic lipid peroxidation, the snake-carrying negative carcinogenic processes in the mammary gland of cows caused by the content of cadmium and lead in secret.

Chamomila recutita

It is quite widespread in all European countries, including Ukraine. The plant is a part of pharmaceutical preparations. The study of the properties of the plant showed that the combined action of azulene and bisabolol has anti-inflammatory activity. Antispasmodic activity has been observed in animal experiments and is associated with the presence of flavonoids and bisabolol. The bitter taste of chamomile is due to the presence of sesquiterpene lactones. The plant's organs contain many biologically active substances, incl. essential oil of blue color, rich in azulene and bisabolol (sesquiterpenes) and polyphenols. The chemical composition of the plant includes a large number of active substances, such as: in essential oil: chamazulene, terpene, sesquiterpenes, cadinene, caprylic and isovaleric acids, apine, prochamisulene, matricena, lactone matcarin, umbeliferon, herniarin, dioxycoumarins, triacanthancholine, phytosterol, salicylic acid, glycerides

of linoleic acid, stalic acid, microscoric acid, microscoric acid, carboxylic acid, carboxylic acid, carboxylic acid, carbohydrate. All these substances played a positive role in reducing the intoxication of the organism of farm animals with heavy metals, especially cadmium and lead, as evidenced by the research results (Tab. 2). The active ingredients of the extract excite the central nervous system and the medulla oblongata, enhance reflex activity, respiration, including its frequency, contribute to a more frequent heart rate, dilate the blood vessels of the brain, the essential oil has disinfecting and anti-inflammatory properties. Glycosides increase gastrointestinal secretion, bile secretion and appetite. Plant glycosides block M cholinoreactive systems, relax smooth muscles, and counteract spasms of the abdominal organs. The organs of the plant through an aqueous extract give an anti-inflammatory effect, relieve spasms of the gastrointestinal tract–one of the significant advantages of this plant in the phytobiopreparation "BP-9", since heavy metals are absorbed through the mucous membranes of the gastrointestinal tract, while the occurrence of inflammatory processes through irritation of cells. The plant is widely recommended for the symptomatic treatment of digestive disorders. Scientists (Mohamed-Amine Jabri et al. 2017) investigated the effect of the extract on rats on glucose absorption in the intestine, a protective role against lipotoxicity, and a reduction in oxidative stress. In the experiment, the diet of the animals had a high lipid content, which led to impaired liver and kidney function. The herbal extract helped to reduce the harmful effects. In our experiment, the active ingredients of the extract prevented digestive disorders and reduced the negative effect of cadmium and lead toxicants on the mucous membrane of the gastrointestinal tract, thereby improving the digestion processes in the body as a result of improving the absorption of the components of another antidote-the mineral and vitamin premix "MP-A" against the background chronic intoxication with toxic metals, constantly entered the body with the diet. The plant is not toxic, but the content of sesquiterpene lactones in the plant can cause allergic reactions (mainly in the form of dermatitis-during scientific and economic experiments and regular examination of experimental cows by a veterinarian was observed).

Eleutherococcus senticosus (Acanthopanax senticosus)

Dutch scientists have established that the root of Eleutherococcus protects some types of living organisms from temperature shock and toxic effects of certain heavy metals (copper and cadmium). Domestic scientists (Gutyj et al. 2016) prove the toxic effect of Cd on several organs, systems, in particular, on the cardiovascular, reproductive, excretory (especially kidneys, liver), respiratory, musculoskeletal system (causes osteodystrophy), hematopoiesis. Indicate a dangerous carcinogenic and mutagenic effect of the element (Gutyj et al. 2016). We have tested the protective effect of the plant extract in toxic metals in scientific and economic experiments on dairy cows. Studies have shown high efficiency of the developed preparation with an extract of this plant, which manifested itself in a stable decrease in the content of cadmium and lead in the milk of cows of the third research groups and an improvement in the quality of the ecological safety of milk as a whole ($p<0.01$). The root of *Eleutherococcus spiny* contains polysaccharides, heteroglycans (eleutherans), which have an immunostimulating effect, eleutherosides A-G (daucosterol, coumarin glycoside, syringaresinol, etc.), I-M (saponins) and other substances. Plant derivatives of coumarin and flavonoids, more than seven eleutherosides. It has a multifaceted effect on the body: it stimulates the central nervous system, increases motor activity and conditioned reflex activity, enhances visual acuity, increases basal metabolism, adaptive properties of the body, lowers blood sugar, increases appetite, has gonadotropic properties (stimulates the adrenal glands). For adult animals, it gives a feeling of cheerfulness, has a positive effect on geodynamic parameters, thereby helping the body to adapt to stress, cold, radiation, as well as the influence of heavy metals, as evidenced by a decrease in their concentration in the liver and kidneys at the end of the experiment in animals of the third research groups ($p<0.01$). Like other plants, it stimulates the immune system, especially its lymphocytic link. This plant is recommended for use with low blood pressure, as well as the prevention of viral infections, in the context of a COVID pandemic, it is especially important. The safety of using the extract requires a professional approach on the part of veterinary specialists and scientists since the plant has many contraindications. For example, it cannot be used for pregnancy, high blood pressure, obesity, rapid heart rate, agitated animals, and the like. We considered all contraindications in the manufacture of a phytopreparation, but the protective effect of this plant on toxic metals is not easy to replace with another species.

Thus, the extract of Eleutherococcus helps to protect the animal's body from the harmful effects of heavy metals and not only Cd and Cu but also Pb, which has been proven by our experiments. Experiments (Donghun Lee et al. 2012) on rats prove the effectiveness of oral administration of Eleutherococcus senticosus to protect against neuronal death in the hippocampus of the brain, explaining this effect by the anti-inflammatory properties of the active substances of the plant and determine the effect of the preparation as neuroprotective. Enhances

the removal of pollutants (Cd, Pb) from blood, milk, internal organs. It normalizes blood pressure, which is very important for dairy cows that experience the toxic impact of xenobiotics, and the immunostimulating effect, resistance to stress and stimulating effect on the adrenal glands contributed to the restoration of the metabolism of mineral substances in the body while increasing resistance to diseases, incl. viral origin, which is often exposed to the body of a productive animal. The results of the experiment showed a high antidote role in the composition of the phytopreparation of this plant.

Salvia officinalis

For the production of the extract, as a rule, in the summer, shortly before the beginning of flowering, or in the fall, the leaves of this perennial plant are collected, which are then dried in the shade. Scientists note that sage affects the production of some neurotransmitters that are necessary for the normal functioning of the brain. The extract of this medicinal plant contributed to the protection of the central nervous system, the functioning of which is blocked by large and small doses of toxic metals, especially cadmium and lead due to the lack of transmission of nerve impulses by disrupting the operation of the corresponding pumps, for example, Ca-Mg-Th, etc., respectively lead to disruption of the brain, the appendages of which produce hormones important for the dairy cow prolactin and oxytocin, which affect the productivity of animals. In acute intoxication with heavy metals, the work of the central nervous system is primarily blocked and the death of the body ends in nervous convulsions. In the introduction of the extract of *Salvia officinalis* into the composition of the phytopreparation, it contributed to the normalization of the functioning of the central nervous system of intoxicated dairy cows. Sage leaves contain flavonoids (1%-3%), triterpenes (oleic, ursular, chlorogenic acids), diterpenes of the abietan type (carnosol, rosmanol, etc.), aromatic acids (rosmarinic acid) and essential oils, which are characterized by the presence of cineole, camphor and monoterpenes of bicyclic ketones. Vitamin P, nicotinic acid, flammable, introduced parades phenol, starch, protein substances, phytoncides, which have strong bactericidal properties. Due to the high content of flavonoids in essential oil, sage relieves intestinal spasms. Ketones exhibit bactericidal and fungicidal properties. Flavonoids, rosmarinic acid and diterpenes have an antioxidant effect. Sage has estrogenic activity, which has been known for a long time but has not yet received an explanation. Sage is recommended for digestive disorders, it is used as a sedative, astringent, hemostatic, anti-inflammatory, choleretic and diuretic. Antimicrobial properties are associated with essential oil, anti-inflammatory with tannins, flavonoid compounds and vitamin P, which thicken epithelial tissues, reduce the penetration of cell membranes, walls of blood and lymph vessels. The antiseptic properties of sage leaves are due to the herbal antibiotic salvin. Salvin not only delays the reproduction of *Staphylococcus aureus,* but also inactivates its alpha-toxin, suppresses its hemolytic and dermatonecrotic properties. This property of sage in the composition of the phytopreparation "BP-9" after injection helped to reduce the bacterial contamination of milk. With mastitis, various microorganisms are found in milk, including bacteria, fungi, yeast, etc. The main causative agents of mastitis are streptococci and staphylococci, which in more than 90% of cases prevail over other microorganisms. Scientists state the fact that earlier the main role in the etiology of mastitis belonged exclusively to streptococci, primarily Str. agalactiae. With the strengthening of the fight against mastitis, the widespread use of antibiotics for their treatment, the situation has changed in favor of staphylococcal infections, the causative agents of which are more resistant to antibiotics and other environmental factors. According to the International Dairy Federation, in most countries, the main role in the etiology of mastitis now belongs to staphylococci. In our studies, we established a subclinical form of mastitis caused by intoxication with heavy metals, therefore, the medicinal properties of sage regarding the delay in the reproduction of Staphylococci and inactivation of their toxins gave a positive effect, observed at the end of the experiment in animals of 3 research groups, where bacterial contamination of milk significantly decreased simultaneously with a decrease in the intake of heavy metals into the mammary gland after the combined use of the antitoxic premix and the biological product "BP-9" in comparison with the animals of the first control groups ($p<0.01$). Sage leaf extract enhances the secretory activity of the gastrointestinal tract, causing a slight antispasmodic effect.

Sage is quite effective for the treatment of inflammatory processes of the genitourinary organs, it is quite possible in village animals with increased elimination of heavy metals in the urine, with mild forms of disturbance of carbohydrate metabolism (observed in experiments). Sage leaves are used for high blood pressure, atherosclerosis, trimtial paralysis. Sage normalizes the glands that produce hormones that promote milk production. Sage extract is recommended to be used for chronic inflammation and metabolic-dystrophic diseases of the joints, therefore the use of sage extract was quite valuable since the violation of mineral metabolism in the body of dairy cows was accompanied by the development of toxic osteodystrophy, which could only be eliminated by a set of measures. Sage extract is also used for diseases of

the liver and kidneys, as a diuretic. Scientists (Yuanyuan Jiang et al. 2017) prove the positive potential of the extract, which has long been used in traditional medicine, for the prevention and treatment of liver cancer, depending on the time of application and concentration. By introducing sage as an additive to water for 21 days (Pogány Simonová et al. 2022), it was possible to change the quality of meat in rabbits. It was these animals that were used by scientists in the experiment. It has been proven that the content of nonessential and non-nonessential amino acids in meat has changed, their number has increased significantly. With short-term use, sage leaf extract does not pose any danger to animal health, but the internal use of sage essential oil is somewhat limited due to the high content of ketones, which have neurotoxic effects. The production of a long-term preparation is the mixing of extracts of various medicinal plants, therefore, the obtained concentration of medicinal sage in the created biological products was acceptable to even for long-term use in intoxicated bodies.

Thus, it is difficult to overestimate the role of sage medicinal extract in the composition of a biological product. In our opinion, the balance of macro and microelements in the body of dairy cows of the third research groups with the cessation of the development of toxic osteodystrophy, which continued to progress in the cows of the first control groups, the normalization of carbohydrate metabolism, a decrease in bacterial contamination of milk due to the natural antibiotic salvin, which counteracts staphylococcal infections, increased bile secretion, with which heavy metals are also removed and an important diuretic effect on the body (acceleration of the elimination of pollutants) could occur without the extract of medicinal sage, the subcutaneous injection of which contributed to the compaction of epithelial tissues and a decrease in the permeability of cell membranes, walls of blood and lymphatic vessels.

Berberis vulgaris

For the preparation of the extract of the common barberry, we used crushed and dried leaves and fruits. The fruits are usually harvested after ripening in September, the leaves in May-June. This plant is quite common in the territory of Ukraine and is well known. Bulgarian researchers in vitro experiments have confirmed the anti-inflammatory activity of berberine, which is found in all parts of the plant. The whole plant contains alkaloids berberine, oxyacanthine, palmitine, moptin, columtin, jatrorricin, berberubin, berbamine (berberine and berbamine have antibacterial properties), essential oil, tannins, high content of vitamins C and E, carotene, malic and citric acid, and coloring matter. The specific gravity of berberine is approximately 3% of the substances contained in the plant. In addition to berberine, fruits contain saponins, organic acids (malic, tartaric) and various sugars. The pharmacological properties of the plant are mainly related to the content of berberine and berbamine, which have antibacterial activity. It has been established that berberine is a chemically active alkaloid capable of forming various modifications. On its basis, preparations are being developed that have specific antitumor and anti-leukemic activity. This is a rather important property of this medicinal plant since the heavy metals cadmium and lead are carcinogenic elements that can cause cancer and leukemia in the body of humans and animals, which is especially dangerous in the production of cow's milk. The studied toxicants can block the work of the tricarboxylic acid cycle in the cells of the body, where the energy molecule ATP is formed, therefore, the content of malic and citric acids in the barberry extract increased the energy capacity of the Krebs cycle. Berberine inhibits the formation of oxygen free radicals and increases the activity of antioxidant enzymes, improves mitochondrial function by reducing the rate of oxygen consumption and increasing the potential membrane against oxidative damage, as proven by studies (Al-Kuraishy et al. 2019). Al-Kuraishy et al. also in experiments on rats proved a positive synergistic role of berberine in attenuating acute kidney damage by various nephrotoxic agents. Since berberine has not yet been synthetically obtained, the biologically active role of the common barberry extract in the phytopreparation only increases. Berberine and berbamine affect the secretion of bile, enhances the elimination of heavy metals through the gastrointestinal tract. Barberry preparations are used as a good tonic, improve appetite and stimulate digestion in the body. Barberry extract is traditionally used for liver failure, has anti-inflammatory properties, promotes rapid blood circulation, lowers body temperature, is anti-microbial, antiseptic, diuretic and choleretic agent, improves blood circulation. The mechanism of action of the preparation from barberry is primarily associated with an antiseptic effect on the gallbladder and a choleretic effect. Barberry extracts are prescribed for cholelithiasis, enlargement of the spleen, disruption of the normal functioning of the liver, incl. inflammatory processes. The use of barberry contributes to the fight against cancerous tumors. The presence of alkaloids determines the certain toxicity of barberry, so it should not be used during the over-feeding period. We injected the preparation into cows during lactation, so the danger of barberry extract is minimal. Thus, it is not difficult to prepare barberry extract on the territory of Ukraine. The extract has a high content of vitamins C

and E, carotene, malic and citric acids, which support the normal functioning of the Krebs cycle. Anticarcinogenic and anti-thyroid preparation. Choleretic and diuretic properties strengthen the antidote protective effect of the preparation "BP-9", about the influence of heavy metals on the body of dairy cows.

Medicago sativa

A perennial herb, which in animal experiments has confirmed its effect on glucose metabolism by lowering its level in the blood. For the preparation of the alfalfa extract, the herb was used, it is harvested at the beginning of flowering, dried and the extract is made. It is widespread in the ecosystems of Ukraine, especially agroecosystems, as it is part of the diets of animals in the form of hay, haylage, etc. Alfalfa is rich in calcium, phosphorus and iron. Contains vitamins A and C, saponosides, cyclic compounds, phytoestrogens (genistein and coumestrol), amino acids, tannins and unsaturated fatty acids. All these active components of the alfalfa extract, somewhat distinguishing it from other medicinal herbs, were included in the composition of the biological product "BP-9". Vitamins A and C are also present in other plants, therefore the preparation "BP-9" itself is quite saturated with these substances, amino acids, calcium, phosphorus and iron contained in alfalfa extract have significantly enriched the preparation, its antidote properties, and the influence of heavy metals have significantly increased. Moreover, the diets of the experimental cows were poor in the content of these elements, the role of sulfhydryl groups of amino acids in the formation of chelated compounds of heavy metals, especially cadmium and lead, and their excretion from the body has already been proven. Alfalfa is effective for its richness in vitamins, amino acids and minerals. The presence of phytoestrogens stachydrin and 1-homostachydrin promotes increased milk secretion, which is especially important both in the production of environmentally friendly milk and in increasing the productivity of cows; Diuretic. In medicine, alfalfa extract is widely used to maintain strength during the recovery period of the body, in the case of urolithiasis of the kidneys, increased lactation, reduce inflammation and as an analgesic agent, it has been proven (Masoud Seddighfar et al. 2020). Today, there is no information about the toxicity of alfalfa, but in any case, its use in the composition of the preparation is best carried out under the supervision of specialists, which was done by us. Thus, the presence of important biologically active substances in alfalfa extract: vitamins A, C, mineral elements Ca, P, Fe, amino acids, unsaturated fatty acids, phytoestrogens make the phytobiopreparation "BP-9" even more effective both in terms of antitoxic effect and to enhance lactation, to maintain the body at the stage of the enhanced removal of toxicants from the body.

Orthosiphon stamineus

A perennial plant whose leaves and flowering tops are collected during flowering, dried, then crushed and extracts are prepared. Observation of patients with nephrolithiasis showed that the use of mink tea extract is quite effective and is not accompanied by side effects. Scientists (Sarshar et al. 2017) show that an aqueous extract from the leaves of the plant prevents bladder and kidney infections in rats. Studies have revealed the intrinsic property of some terpene compounds extracted from the plant to stop the division of cancer cells. The active substances of the plant extract enhanced the excretory function of the kidneys, associated with the elimination of toxic metals, and contributed to the restoration of the normal function of the renal tubules and nephrons. An important role belongs to polyphenols and, especially, flavonoids, including sinenzetin. These are lipophilic compounds in contrast to the water-soluble flavone heterosides. In this regard, the active substances of the plant can easily overcome the lipid membrane of cells, which means that the effect of forecasting is achieved by us. Kidney tea leaves contain the bitter glycoside orthosiphonin, soluble in water, in a small number of alkaloids, triterpene saponins, fatty oil, tannins, organic acids, essential oil, beta-sitosterol, a large number of potassium salts, the role of the latter in the transport of substances into the cell sodium-potassium pump of cadmium and lead intoxication is simply invaluable. In experiments on animals, an increase in diuresis was proved after the application of the extract of renal tea. The aqueous extract is capable of enhanced excretion of ions, including heavy metals. Flavonoids can scavenge free radicals. Clinical observations have shown that along with increased excretion of fluid, an intensive removal of urea and uric acid, chlorides occur. A positive effect in improving the body from nephrolithiasis. Kidney tea is recommended for use in case of insufficiency of the gallbladder, with the formation of salts in the kidneys and gallbladder, with poor urination. Thus, renal tea is a strong diuretic-diuresis double, the removal of chlorides by 39%, lead excretion in experimental studies on animals increased by 25%. Moreover, the withdrawal of lead begins about 5 days earlier than without its use. Kidney tea is used for acute and chronic kidney disease, accompanied by edema, albuminuria, azotemia, and the like. Kidney tea helps to increase glomerular infiltration and improve renal tubular function. Already a few days after the application of the extract, urine alkalinization may occur, that is, the pH changes from an acidic medium to an alkaline one, which is confirmed by our

studies of animal urine. After using renal tea, appetite improves, the amount of mucus and leukocytes in bile significantly decreases, secretion in the gastrointestinal tract increases, which means that digestion processes improve. The aqueous extract helped to increase milk production. The plant itself has a very good affinity for other medicinal plants that have diuretic and anti-inflammatory properties, therefore, without restrictions, it can be included in various preparations, incl. and the biological product "BP-9" developed by us. There is no information on the toxicity of this plant during its use in therapeutic doses, on the contrary, the extract is effective with prolonged use, even with minor interruptions, doesn't have any side effects.

So, the positive role of the extract of this plant in the composition of the biological product is obvious. Our experiments, as well as the experiments of other scientists, have shown an increase in the removal of lead and cadmium. In the experimental cows, proteinuria was observed, which disappeared after the injection of the herbal preparation, and here the extract of renal tea undoubtedly worked, since protein reabsorption was restored in the renal tubules. The excretion of cadmium and lead in the urine without degenerative changes in the kidneys is a positive in the study of the extract of this plant. The role of the extract of kidney tea in the composition of the biological product "BP-9" can be called decisive.

Hyppophae rhamnoides

A natural source of vitamins, primarily vitamin C, has played an important role in the intoxication of the body with cadmium, lead and other heavy metals. For the manufacture of the extract, we used sea buckthorn fruits. The plant itself is widespread in Ukraine, so the preparation of medicinal substances from it is not difficult. The composition of the active substances of this plant also includes the oily fraction of vitamin F, which consists mainly of saturated and monounsaturated fatty acids, facilitated the delivery of the ligand groups of the preparation through the cell membranes. Contains vitamin E and oil enriched with polyunsaturated fatty acids (linolenic and alpha-linolenic). Fruits contain up to 8% fatty oil, up to 12% ascorbic acid (vitamin C), B1, B2, K, P, carotenoids, folic acid, choline, betaine, coumarins, phospholipids, sterols, triterpene substances, carbohydrates (glucose, sucrose, fructose, pectin, polysaccharides), cyclitol quebrachite, organic acids, phenol carboxylic acids, flavonoids, leukoanthocyanins, tannins, macro-, microelements (sodium, magnesium, silicon, iron, aluminum, calcium, nickel, molybdenum, manganese, etc.). Scientists (Yankun Hao et al. 2020) have proven the positive role of the flavonoids of the *Hippophae rhamnoides* extract in protecting the liver of animals from fatty degeneration. There is no ascorbinase, which ensures a good preservation of ascorbic acid. Sea buckthorn extract is a significant source of vitamins. Vitamin C provided the body's resistance to infectious diseases, collagen synthesis and iron absorption in the gastrointestinal tract. In addition, vitamin C, like vitamin E, carotene and flavonoids, is a natural antioxidant that has protected the body from free radicals. For sea buckthorn, anti-inflammatory, bactericidal, wound healing, heat-sore, epithelizing properties are also characteristic, the latter is especially important, since heavy metals cadmium and lead can irritate the epithelial tissues of the udder of cows, which leads to an increase in the content of somatic cells in milk, increases the body's resistance to ionizing radiation, prevents malignant tumors in the gastrointestinal tract. Affects lipid metabolism in blood serum, normalizes blood pressure, strengthens the walls of blood vessels, has a positive effect on bilk synthesis function of the liver, reduces fat content in fatty liver infiltration, indicates the development of hypoglycemia and hyperlipidemia, stabilizes the activity of several enzymes, the work of which is blocked by heavy metals, especially damage to their active part, reduces the development of dystrophic and necrotic changes in the liver and other organs, quite likely due to intoxication with cadmium and lead, stimulates reparative processes. It makes it possible to eliminate hypovitaminosis, which is very important with the increased pressure of heavy metals on the organs and systems of the body. It is recommended for the treatment of toxic effects of the liver, therefore, the inclusion of this plant in the composition of a biological product is undoubtedly true. The fruits contain malic, tartaric, niacin and essential oils. In this regard, sea buckthorn extract enhances the secretion of gastric juices. There are no restrictions on the use of sea buckthorn extract.

So, one of all the medicinal plants we have considered does not have such poly-vitaminization and mineralization as sea buckthorn vitamins C, E, B1, B2, K, P, even F, and among the mineral elements sodium, magnesium, silicon, iron, aluminum, calcium , nickel, molybdenum, manganese, etc., the range of therapeutic effects is also impressive, among the characteristic of other plants, sea buckthorn is characterized by an epithelizing function– for the restoration of the epithelium of the udder of cows, it played an important role, the normalization of protein and lipid metabolism with a simultaneous restoration of the content lipids in the blood, a positive effect on the protein-synthesizing function of the liver, which undergoes a toxic shock from cadmium and lead; strengthening the walls of blood vessels, where

heavy metals are transferred with the blood flow, being absorbed into the blood in the gastrointestinal tract, stabilizing the work of the enzymatic system, preventing dystrophic and necrotic changes in the liver, which can be caused by cadmium, and this is not the end of the positive medicinal role of sea buckthorn.

Verbena officinalis

Modern pharmacological studies have revealed the immunostimulating effect of this plant, some of its components interact with prostaglandins-mediators of cellular activity. The introduction of a plant with a pronounced immunostimulating effect into the composition of a biological product was extremely necessary since the toxic effect of heavy metals leads to a decrease in the body's resistance and the immunodepression state of animals arises, accompanied by a decrease in gamma globulin fractions in the blood, which carries antibodies, was observed by us during morpho-biochemical studies of the blood of cows, especially the first control groups both at the beginning and at the end of the experiment. The inflorescences contain iridoids (including verbenaloside), beta-sisterol, triterpenes, mucous substances and flavones, which have an antispasmodic and anti-inflammatory effect, which reduced inflammation in the udder of cows caused by the influence of heavy metals, as well as the kidneys and liver, where tubules, nephrons and hepatocytes are affected. Verbena has anti-inflammatory and antispasmodic effects. Especially, it should be noted its property to relax the uterine muscles. Some of its components strengthen the immune system by stimulating the production of interleukin. It has shown its hormone-like activity, affecting lactation and inhibiting thyroid-stimulating hormones. It is possible that the last medicinal properties of verbena turned out to be one of the key ones since xenobiotics suppress the hormonal system of the body, which immediately affects the lactation process. At the beginning of the research period, the productivity of cows was at the level of 14.0 kg-15.5 kg, at the end of the experiment it increased in the third research group to 18.4 kg-22.6 kg, and in the first control groups the lactation process generally worsened, the productivity of cows became even less than it was at the beginning of the experiment. Today, vervain has proven to be effective against digestive disorders, it is recommended to enhance lactation. Scientists (Sau-Wan Lai et al. 2006) indicate a significant potential for the cytoprotective action of an aqueous extract of *Verbena officinalis* on cells of the central nervous system. There are no reports of its toxic effect even after six months of use.

Consequently, this medicinal plant in the composition of the biological product "BP-9" was responsible for the immunostimulating and hormone-stimulating effect in the body, improvement of the lactation process, and hence the formation and secretion of milk. It does not have toxic properties and a limiting period of use. It makes it possible to establish the most effective injection doses of the preparation and to inject it for prophylactic purposes for a significant period, or rather, during the entire lactation period, before the onset of the dry period. For the body of dairy cows, in fact, like other animal species, it is important to have a significant amount of mineral elements, vitamins, organic acids and many other useful substances, the main ones are oxygen, carbon, calcium, phosphorus, sodium, chlorine, magnesium, fluorine, hydrogen, potassium, iron, molybdenum, selenium, silicon, nitrogen, sulfur, iodine, manganese, even such as arsenic in small amounts can activate metabolic processes in the body, etc.

In general, in the world, there is a lot of successful experience in the use of extracts of medicinal plants, proven by many complex experiments. Scientists (Milton Prabu, et al. 2012) studied the leaf extract of the perennial evergreen betel nut (Latin Piper betie) and obtained a good protective effect against Cd-induced oxidative liver damage in rats. Other scientists (Fan, et al. 2018) used betulinic acid, a natural pentacyclic triterpenoid found in the bark of some plant species, birch (Betula pubescens), to remove cadmium in animals. Betulinic acid exhibited combustible and cancer-protective properties increased the excretion of Cd from the liver and kidneys, the concentration of Cd in the urine increased, which proves the excretion function of the active substance in the herbal preparation (Fan, et al. 2018). A good result in dosages for intoxication with cadmium and lead was given by an aqueous solution of tannic acid, which many plants contain (Winiarska-Mieczan, 2013), mangosteen extract (an evergreen tree from Latin Garcinia Mangostana) relieves Pb-induced neurotoxicity (Phyu & Tangpong, 2014). Also, bilberry extract (*Vaccinium corymbosum* L.), isolated anthocyanins have a protective, therapeutic effect against cadmium intoxication at the level of metal-chelating complexes (Gong, et al. 2014). *Physalis peruvian* (Cape Kryzhovnik-Latin Physalis peruviana) of the *Solanaceae* family, in the experiment, completely changed the histopathological state of the liver and kidney tissues. Scientists (Dkhil, et al. 2014) have proven its good hepatorenal protective role, decreases lipid peroxidation, and the like. In the liver and kidney of cows of the second research group of cows and especially the first control groups, where the herbal preparation was not used, the highest content of toxic metals was recorded, which proves the accumulating effect of

pollutants. The concentration of pollutants in these very organs, in animals of the second research group, tended to decrease due to the blocking effect of toxicants in the gastrointestinal tract using the antidote mineral and vitamin premix "MP-A", which significantly changed the metabolism in the body (P<0.01). In animals of the first control groups, the kidneys and liver were organs of enhanced accumulation of toxic metals (p<0.01).

We managed to balance the content of several mineral elements in the body of cows using a premix based on the synergistic and antagonistic action between the elements. When developing the biologically active preparation "BP-9", we adhered to similar approaches. It was taken into account repeated and its multiple uses for the accumulation of the active substance (ligand groups) in the tissues of the body (material cumulation) with the summation of pharmacological substances (cumulation of the effect). Material cumulation-the preparation for repeated administration does not have time to be inactivated in the process of biotransformation or be excreted from the body, as a result of exceeding therapeutic doses or reducing the time between doses. This property is possessed by substances capable of forming stable complexes mainly with proteins of blood plasma, cell membrane or cytoplasm (heavy metals, arsenic, bromine, iodine and some others). Fat-soluble compounds can accumulate in the reserves of neutral fat and in lipoproteins, which are especially rich in the nervous tissue and internal organs. The cumulation of the effect of plant components caused persistent changes in the structural components of cells under the influence of antitoxic, medicinal substances they are not restored until repeated use, although the substance itself does not stay in the body for a long time. As a result, we received a positive effect from the repeated use of the herbal preparation, which affected the productivity of cows, the quality of milk, its environmental safety and the health of animals as a whole. The complex action of medicinal substances is the most effective since it involves the simultaneous use of not one, but several preparations acting on various organs and systems, and at the same time complement each other than expanding the protective antitoxic and pharmacological effect. The content in the preparation of plants that have a similar effect and act in the same direction-their synergistic action is manifested. The preparation and its herbal components undoubtedly exhibited both physical and chemical antagonism. Under physical antagonism, the use of enterosorbents and ligand groups of substances is manifested, which contribute to the neutralization and elimination of toxicants from the body, chemical antagonism of the preparation appears with the loss of toxic activity by heavy metals due to the formation of new inactive (chelate) compounds. In the tissues of the body, sulfhydryl and carboxyl compounds of the preparation can form stable chelate complexes with heavy metals and remove them from the body.

The mass ratio of extracts of medicinal plants in the biological product "BP-9" (see above) was established depending on the available biologically active substances in each of the extracts of medicinal plants included in the chemical composition of the preparation "BP-9". At the same time, in the first place were such properties as restoring the balance of macro-and microelements in the body of dairy cows, stopping the development of toxic osteodystrophy, normalizing carbohydrate, protein, lipid metabolism, reducing bacterial contamination of milk due to the natural antibiotic salvin, which counteracts staphylococcal infection, increased bile secretion with which heavy metals are removed, a diuretic effect on the body (acceleration of the elimination of pollutants), which could have happened without the extract of medicinal sage, the subcutaneous injection of which contributed to the compaction of epithelial tissues and a decrease in the permeability of cell membranes, walls of blood and lymphatic vessels, therefore its share in the preparation "BP -9 "was 17 ml or 17%. Further, in the same percentage by weight, extracts of *Schisandra chinensis, Eleutherococcus prickly*, kidney tea and buckthorn (15 ml or 15% each) were taken, which play an equally important antidote role in the composition of the phytobiopreparation "BP-9". Lemongrass extract protected the liver, kidneys, spleen, heart, lungs from the toxic effects of heavy metals, in addition, reduced the negative carcinogenic processes in the mammary gland associated with the migration of cadmium and lead into the blood and milk, preventing the oxidation of hepatic lipids, the extract of *Eleutherococcus* helped to protect the animal's body from the harmful effects of heavy metals, proved by experiment activated the intensity of the removal of pollutants from blood, milk, internal organs and body systems. Normalized blood pressure, immunostimulating effect, resistance to stress and stimulating effect on the adrenal glands, contributed to the restoration of mineral metabolism in the body while increasing resistance to various diseases, incl. viral origin; extract of renal tea enhanced the excretion of cadmium, lead, copper and zinc, was confirmed by experiments, effectively counteracted the development of proteinuria, helped to restore the functioning of the renal tubules and glomeruli of infiltration, prevented degenerative changes in this important organ during intoxication; sea buckthorn extract having a large set of vitamins and mineral elements (vitamins C, E, B1, B2,

K, PP, even F, mineral elements sodium, magnesium, silicon, iron, aluminum, calcium, nickel, molybdenum, manganese, etc.) supported the body of animals at the stage of restoring homeostasis, when a significant amount of toxicants began to be eliminated from the body, an extremely important epithelizing function contributed to the restoration of the epithelium of the udder of cows, which influenced a decrease in the content of somatic cells ($p<0.01$). Improvement of the protein-synthetic function of the liver, strengthening of the walls of blood vessels, stabilization of the work of the enzymatic system, reduction of dystrophic and necrotic changes in the liver, and several other important signs. It seemed somewhat more important to us the role of barberry in the composition of the developed biological product, which in terms of mass ratio took the third place 12 ml or 12%, which is again determined by active substances, high content of vitamins C and E, carotene, malic and citric acids, support normal functioning the Krebs cycle.

Anticarcinogenic and anti-thyroid preparation

Choleretic and diuretic properties only strengthen the antidote effect of the preparation "BP-9", about the effect of heavy metals on the body of dairy cows, in addition, it is not difficult to prepare an extract from this plant, since it is very widespread in Ukraine, in fact, like most medicinal plants of the preparation, in the amount of 5% by weight or 5 ml, alfalfa extract was introduced; it also has an increased content of vitamins A, C, mineral elements Ca, P, Fe, amino acids, unsaturated fatty acids, phytoestrogens and enhances lactation; and in an amount of 3% or 3 ml, chamomile and *Verbena officinalis* extract was introduced. The widespread prevalence of plants in various ecosystems of Ukraine, proven medicinal properties to reduce the toxic effects of heavy metals on the organism of farm animals, activation of digestion processes and a decrease in inflammation of the mucous membrane of the gastrointestinal tract, immunostimulating and hormone-stimulating effect, improvement of the lactation process, the absence of a limiting period of use made it possible to establish the most effective doses of injection of the preparation "BP-9" (see above) and to inject it for a prophylactic purpose for a sufficiently long period (during the entire period of lactation), before the onset of the dry period.

Thus, the biological preparation "BP-9" contains a significant amount of fat-soluble substances, weak electrolytes are quickly reabsorbed in the renal tubules, which means that the ligands of the preparation group are delivered directly to the cells of organs and tissues, which contributes to the formation of chelate complexes with heavy metals in them and their excretion from the body. When released faster, they can transform into more polar components as more ionized and less soluble metabolites, they become less able to be deposited in fats, bind to plasma and tissue proteins, and in smaller quantities penetrate cell membranes. This type of biotransformation is called the inactivation of toxic substances. After using the preparation, other pharmacologically active structures can be formed in the process of metabolism, but they are also further biotransformed or excreted in the form of active metabolites in the urine. The metabolism of the active substances of the preparation occurs mainly in the liver, but can also be found in blood plasma, kidneys and other tissues.

The active substances of the preparation act as chelating agents in the body. Most active substances are capable of being good ligands. Each potential chelating agent competes for a metal ion with many other ligands. There are cases where the antitoxic and therapeutic effect of a substance can be attributed to the control or inhibition of an enzyme through the chelation of a metal ion. The active substances of the preparation inhibit the enzyme that interacts with heavy metals and disrupts the formation of the combination of heavy metals with the enzyme at the stage of its formation, and further affect the deterioration of the absorption of toxicants in the gastrointestinal tract. Since the formation of a complex with a metal ion can lead to the formation of a neutral fat-soluble particle capable of permeating the cell membrane. The metal ion thus acts as a carrier of the preparation.

Having in its composition all the necessary mineral elements: iron, selenium, molybdenum, boron, calcium, chromium, fluorine, sodium, lithium, iodine, silicon, manganese, copper, zinc, nickel, vanadium, bromine, cobalt, incl. antagonists of heavy metals cadmium and lead, and among vitamins A, C, B, P, E, K, F (Tab. 1) with the help of phytopreparation injection we were able to enhance the antitoxic effect of the mineral-vitamin premix "MP-A" at the tissue level, organs and systems of intoxicated cows.

Conclusions

Feeding dairy cows with a mineral and vitamin premix promoted the elimination of heavy metals at the metabolic level due to the elements of heavy metal antagonists, which are capable of replacing (displacing) toxic metals cadmium and lead in metabolic processes at the level of the gastrointestinal tract, sodium succinate and citric acid normalized the cycle tricarboxylic acids, and the biologically active phytopreparation "BP-9" from the extract of medicinal plants enhanced the antidote properties of the premix by acting as a protector

directly in the tissues and organs of the cows of the third research groups, forming compounds with heavy metals and delivering them to the excretory organs. A positive synergistic effect has been achieved between the premix and phytopreparation, the key role belongs to the active substances of aqueous extracts of successfully selected medicinal plants, has comprehensively provided a good protective effect of the body of lactating cows under conditions of chronic Cd, Pb intoxication with the production of environmentally friendly milk and the preservation of the health of farm animals.

The use of phytopreparation and premix will ensure the production of environmentally friendly cow's milk with toxic metals within the permissible norms in farms that are in conditions of increased anthropogenic pollution of agroecosystems, including around developed industrial cities.

Further research is aimed at the selection of medicinal plants with the best protective, phytomorphological and biochemical properties to the action of toxic metals, radionuclides, improvement of the developed antidote substances and methods of their use in animal husbandry.

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