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Cow's milk screening for veterinary drug and pollutant residues in Ukraine for the period from 2020 to 2023

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ABSTRACT

Dairy industry is leading in the structure of the food industry of Ukraine at the current stage. It consists of the butter production, cheese production, and milk-canning sub-sectors, as well as manufacturing of whole milk products, since the products of this industry occupy an important place in the consumption of the population. Therefore, research on regulation, toxicological and hygienic assessment of toxic contaminants of various origins must be conducted. The purpose of this study was to assess the cow's milk from Ukrainian farms for the presence of key safety indicators over the past 4 years, namely: residues of antibiotics, nitrofurans, coccidiostats, insecticides, fungicides, anthelmintics, corticosteroids, glucocorticosteroids, organochlorine and organophosphate pesticides, mycotoxins, toxic elements, radionuclides. In the period of 2020-2023, 7138 samples of cow's milk from native dairy enterprises from 25 regions of Ukraine were screened for the content of various dangerous substances and compounds from groups A and B which are declared in Directive 96/23/EC. It was established that the milk of cows from Ukraine meets current national standards and is not inferior in terms of quality and safety to EU indicators. Among the inconsistent results, it is worth highlighting the presence of Chloramphenicol in 0.85% of milk samples out of 234 tested for its content, which was 0.03% of the total number of samples, while the content of other investigated drugs and substances was below of the methods detection limit.

Introduction

The safety of food products and food raw materials is one of the decisive components of the economic security of every state, and it determined by the country's ability to effectively controlled the production and import of safe and high-quality food based on universally recognized principles. It can be called a historical phenomenon that quality (as a category) is a national idea of all developed countries of the world. Therefore, research on regulation, toxicological and hygienic assessment of toxic contaminants of various origins is widely conducted in the countries of Europe, Asia, and America (Uçar *et al*., 2016; Vågsholm *et al*., 2020; Tsoukas *et al*., 2022).

Dairy industry is leading in the structure of the food industry of Ukraine at the current stage. It consists of the butter production, cheese production, and milk-canning sub-sectors, as well as manufacturing of whole milk products, since the products of this industry occupy an important place in the consumption of the population: share of expenditure on dairy products is 15.0% of total food expenses (it ranks fourth after expenses for bakery, meat, flour, and pasta products) (Dzhedzhula *et al*., 2018; Hladiy and Prosovych, 2022).

Ensuring product quality, safety and competitiveness is the main factor for dairy industry development under conditions of a market economy. In the process of production and meeting the demand of the population, the requirements for the quality characteristics of dairy products are constantly increasing, and HACCP is the most effective system that allows ensuring food product safety and quality during the production of raw materials, processing, storage, transportation, and use. ISO standards, actively implemented by Ukrainian milk processing enterprises, have also become guarantors of product quality (Odarchenko *et al*., 2016; Golovko *et al*., 2021). These standards regulate key indicators, in particular, milk safety, namely: quantitative content of nitrofurans, nitroimidazoles and other A2 substances, antimicrobial agents, insecticides, fungicides, anthelmintics and other antiparasitic agents, non-steroidal anti-inflammatory agents, corticosteroids and glucocorticoids, some organochlorine and organophosphate compounds, heavy metals, mycotoxins and radionuclides.

The need to control these compounds in livestock products, including milk, is due to several factors described below. Thus, nitrofurans are antimicrobial agents prohibited for use in food-producing animals in the European Union, because nitrofurans and their marker metabolites, as a rule, have genotoxic and carcinogenic properties (EFSA CONTAM Panel, 2015).

Annually, 63151±1560 tons of antibiotics are used in animal industry worldwide to stimulate growth and treat livestock, leading to the release of their significant amount through milk in an unchanged form and causing serious harm to human health and emergence of antibiotic-resistant bacterial strains (Sachi *et al*., 2019).

Long-term preservation of the residual concentration of various antiparasitic agents in milk should be taken into account when treating animals during the lactation period. The high lipophilicity of some of the most widely used antiparasitic agents accounts for their high distribution in milk and the long-term persistence of high residual concentrations in milk after processing. Most of the studied antiparasitic medicinal compounds proved to be stable in various industrial processes related to milk, including fermentation and pasteurization (Imperiale and Lanusse, 2021).

The use of corticosteroids and anabolic steroids in food producing animals is regulated or banned in the European Union (EU). However, their use as growth promoters cannot be excluded. Milk replacers, considered by EU legislation as feeds, may be a good way of administration of these compounds (Chiesa *et al*., 2016). The presence of steroid hormones in milk can be one of the factors in hormonal imbalance and its consequences in a human consuming such milk: a decrease in the level of testosterone and pituitary gonadotropins, prostate cancer in men; endometrial and ovarian cancer in women (Nili-Ahmadabadi *et al*., 2021).

The issue of residues of organochlorine and organophosphate compounds in milk is also relevant, although they have been banned for use in agriculture since the 1980s, because the half-life of some representatives of this group exceeds 30 years. At the current stage, it is believed that these compounds have a general toxic, polytropic effect on the body, and due to the lipophilic nature of organochlorine compounds, they are mainly neurotoxic and parenchymatous (hepatotoxic) poisons (Silva *et al.*, 2014; Rêgo *et al.*, 2019).

Heavy metals are commonly found in nature and their concentrations in food items are increasing day by day as a result of utilization of untreated sewage water and industrial effluents for irrigation of crops. Animals are reported as efficient filter of metals, and as a result minute quantities are naturally added to milk through animal bodies. Metals may contaminate animal milk through instruments and machinery used in processing and distribution of milk. For this reason, processed milk is reported to have higher concentrations of heavy metals as compared to raw milk. Furthermore, heavy metals may also enter into milk through contaminated animal feed by the routes of irrigation with polluted canal or sewage water, the application of pesticides and fungicides, and the presence of industries near the animal feed areas (Ismail *et al.*, 2017; Yan *et al.*, 2022).

Regarding mycotoxins in milk, the leading place is occupied by the main metabolite of mycotoxin B1 – mycotoxin M1, which is a strong immunosuppressant for humans and exhibits mutagenic and carcinogenic properties (Admasu *et al.*, 2020; Hassouna *et al.*, 2023).

The study of the content of radionuclides in milk is especially relevant in Ukraine due to the disaster at the Chernobyl NPP almost 40 years ago, and the negative effect of radioactive compounds on the human body is well known (Lesyk *et al.*, 2012; Kochetova *et al.*, 2020).

However, recently, the dairy industry development has been adversely affected by several additional factors that significantly worsen the provision of milk quality and safety, namely: COVID-19 pandemic, imposition of martial law and active military actions on the territory of Ukraine, which determined the purpose of our study – to screen the key milk safety indicators in Ukraine for the period 2020-2023.

Materials and methods

The studies were carried out in the scientific-research chemical and toxicological department, State Scientific Research Institute of Laboratory Diagnostics and Veterinary and Sanitary Expertise, Kyiv, Ukraine.

Sample collection

For the period from 2020 to 2023, 7138 cow's milk samples from domestic dairy enterprises of 25 regions of Ukraine were tested for the presence of residues of antibiotics, nitrofurans, coccidiostats, insecticides, fungicides, anthelmintics, corticosteroids, glucocorticosteroids, organochlorine and organophosphate pesticides, mycotoxins, toxic elements, radionuclides. Samples for testing were collected by regional veterinary inspectors in accordance with the methodological recommendations on sampling procedure for the implementation of the State Plan for monitoring of veterinary drug and pollutant residues in live animals and unprocessed food products of animal origin in Ukraine (taking into account the requirements of Council Directive 96/23/EC). The number of collected samples and the number of investigated dairy farms were determined annually by specialists of the State Service of Ukraine on Food Safety and Consumer Protection and state inspectors at the territorial level. The selection of collected samples was determined taking into account breed and age; volume of milk production in farms; animal husbandry and breeding technologies; presence of facts of non-compliance with requirements in the past, including receiving inappropriate results of laboratory tests, violation of legislation requirements during the implementation of a previous scheduled or unscheduled measure of state control; use of veterinary drugs and medicated feeds, non-observance of elimination (withdrawal) periods. Milk samples in the amount of 500 ml were collected at dairy farms in a sterile plastic container, sealed and cooled to +2 to +7 °C, thereafter, they were delivered to an authorized laboratory for testing within 36 hours. If the delivery time was longer, raw milk samples were frozen and stored at -18°C for a week.

Analytical analysis

Two-dimensional liquid chromatograph coupled to mass spectrometer Alliance XE and Xevo (Waters Corporation, USA) equipped with analytical SunFire™ C18 column, 5 µm, 4.6×50 mm for Alliance XE and ACQUITY UPLC® BEH C18, 1.7 µm, 2.1×100 mm for Xevo, dual quadrupole tandem mass spectrometry detector, positive ionization electrosprayer and MassLynx calculation software were used to test the residual content of antibacterial drugs in milk. For internal quality control of testing...

Measurement of the mass fraction of multiresidue pesticides in milk was carried out using GC/DES method after their appropriate extraction from the sample with solvents, purification of the extract in the liquid/liquid system and/or using chromatographic column packed with Florisil sorbent. Identification was carried out based on retention time, when using GC-MS based on the presence of relevant ions and their intensity ratio, and quantitative determination was performed using the external standard method based on peak area. For this purpose, a gas chromatograph Varian GC-450 with an electron capture detector and an autosampler, and standard samples of the pesticide composition of Sigma-Aldrich company with a purity of 99.9% were used. To control the testing quality, return tests (sample with an additive) were performed, adding pesticides to the sample with a concentration according to the MRL/LoQ in terms of weight. System sensitivity was also evaluated according to one of the calibration solutions. Test reproducibility was controlled using a duplicate sample.

Content of aflatoxins M1 was determined using HPLC method with immunoaffinity chromatography in accordance with ISO 14501:2007 using a liquid chromatograph with a fluorescent detector and using an analytical reverse-phase column S 250 x 4.6 mm, 100 - 5 C18, immunoaffinity RIDA® Aflatoxin columns. Acetornitrile 60% and water 40% for HPLC, Merck (Germany), were used as the mobile phase. Aflatoxin M1 standard, 10 µg/ml, acetonitrile solution, Sigma (Germany). Sample was prepared using centrifugation at a radial acceleration of 3000 rpm for 10 minutes, fat removal followed by immunoaffinity chromatography using immunoaffinity columns. Elution was carried out with methanol followed by washing with water. Blank sample, standard solution (1ng/ml) and internal reference material with the addition of a standard solution were used for internal quality control.

Atomic absorption spectrometry with electrothermal atomization (Thermo Solaar, USA) was used to determine lead and cadmium in accordance with ISO 11212-3:1977, Determination of lead content by atomic absorption spectrometry with electrothermal atomization and ISO 11212-4:1977, Determination of cadmium content by atomic absorption spectrometry with electrothermal atomization. Atomic absorption spectrometry with a direct sample injection system (Milestone DMA-80, Italy) was used to determine mercury in accordance with ISO 11212 - 2:1997 (E) Part 2 Determination of mercury content by atomic absorption spectrometry. Merck (Germany) working single-element standard solutions for atomic absorption spectrometry with certified ion content were prepared by diluting them in such a way as to obtain concentrations of the same order as the upper limits of the element content range. 2% Merck (Germany) nitric acid solution was used to dilute the standard solutions. Sample preparation was carried out according to the following scheme: 2 cm3 of nitric acid was added to a 5 ml sample and subjected to microwave decomposition. Determination of mercury was carried out by the direct method without preliminary preparation of the sample. Certified reference material - TFV002RM - Milk Powder with certified content of cadmium, lead, mercury analytes (Fapas, UK) was used for internal quality control.

All used methods for determining pollutants are validated in accordance with Commission Implementing Regulation (EU) 2021/808 of 22 March 2021 on the performance of analytical methods for residues of pharmacologically active substances used in food-producing animals and on the interpretation of results as well as on the methods to be used for sampling and repealing Decisions 2002/657/EC and 98/179/EC and accredited for compliance with the requirements of the DSTU EN ISO/IEC 17025:2019 standard.

Statistical analysis

For statistical processing of data, the software package for analysis of variance (ANOVA) StatPlus (7.6.5.0) (AnalystSoft Inc., USA) was used.

Results

Milk screening results for chloramphenicol and nitro-group-containing drugs are demonstrated in Table 1. A total of 1664 samples of cow's milk were tested for these indicators during the reporting period. Ninety-nine milk samples were tested for the presence of dapsone and chlorpromazine from the Other A2 Substances group over the years, but these drugs were not detected in any sample (Table 1).

Milk was tested for such nitroimidazoles as ronidazole, dimetridazole, metronidazole, ipronidazole, ipronidazole-OH (PZOH), metronidazole-OH (VNZOH), ternidazole and hydroxy dimetridazole (HMMNI). A total of eighty samples were studied, and no residual amounts of the corresponding drugs were found in any milk sample. Also, in 2020-2023, no nitrofurans (AOZ, AMOZ, SEM and AHD) were found in cow's milk – 148 samples were tested for each. While chloramphenicol was detected in 2 out of 234 milk samples (in one sample in 2020 and one in 2023, the corresponding concentrations were 0.284 and 1.86 μg/l), which was 0.85% of the samples tested for chloramphenicol and 0.12% of the total number of samples (Table 1).

Cow's milk screening results for antimicrobials are demonstrated in Table 2. Thus, in the period from 2020 to 2023, 3584 milk samples were tested for antimicrobials. Over the years, eighty-eight milk samples were tested for such penicillins as benzylpenicillin, amoxicillin, ampicillin and ninety-six samples for cloxacillin, but these drugs were not detected in any sample (Table 2). Furthermore, no florfenicol residual amounts were found in eighty-eight milk samples (Table 2). Over the past four years, 101 milk samples were tested for tetracycline antimicrobials (tetracycline, chlortetracycline, oxytetracycline and doxycycline), and no residual amounts were found (Table 2).

During 2020-2023, such aminoglycosides as kanamycin, apramycin, streptomycin, dihydrostreptomycin, spectinomycin, gentamicin and neomycin were found in ninety-six milk samples, but their residues were not detected. Fluoroquinolones (enrofloxacin – ninety-six samples, norfloxacin – ninety-eight, ciprofloxacin – ninety-eight and flumequin – ninety-eight samples) were not found in milk during the reporting period (Table 2). Furthermore, no sulfonamides were found in milk samples (eighty-eigh samples were tested for sulfathiazole, ninety-nine samples for sulfadimethoxine, sulfaguanidine, sulfadiazine, sulfamerazine, sulfamethazine (sulfadimedine), sulfamethoxypyridazine each, respectively, ninety-six samples for sulfamethoxazole, sulfanilamide each, respectively) (Table 2). Milk was tested for antimicrobial drugs of other groups: erythromycin, tylosin, lincomycin, colistin – eighty-eight samples each, trimethoprim, ceftiofur, cefquin, cephalexin, tiamulin – ninety-six samples each, respectively, however the residual amounts of the drugs were not found (Table 2).

Cow's milk screening results for antiparasitic agents are demonstrated in Table 3. Thus, in the period from 2020 to 2023, 653 milk samples were tested for antiparasitic agents.

During 2020-2023, milk was tested for such anthelmintics as albendazole, fenbendazole, levamisole, clorsulon, closantel, mebendazole, oxyclozanide, rafoxanide, and triclabendazole (fifty samples were tested in total), but no residual amounts of these drugs were found in any sample.

Table 1. Ukrainian cow's milk screening results for chloramphenicol and nitro-group-containing drugs for 2020-2023, μg/l.

Chemical Group		Number of tested samples by year			Detection Limit (method)	Number of positive samples	Determined concentration	Maximum residue limit*
		2020-2021	2022	2023				
Chloramphenicol		60	143	31	<0.1	2	0.284±0,001 1.86±0,02	Not permitted
Nitrofurans	AOZ - furazolidone, which is metabolized to 3-amino-2-oxazolidinone	60	57	31	<0.54	0	<0.54	
	AMOZ - furaltadone, which is metabolized to 3-amino-5-morpholinomethyl-2-oxazolidinone	60	57	31	<0.52	0	<0.52	
	SEM - nitrofurazone, which is metabolized into semicarbazide	60	57	31	<0.52	0	<0.52	
	AHD - nitrofurantoin, which is metabolized to 1-aminohydantoin	60	57	31	<0.57	0	<0.57	
Nitroimidazoles	Ronidazole	30	28	22	<1.0	0	<1.0	
	Dimetridazole	30	28	22	<1.0	0	<1.0	
	Metronidazole	30	28	22	<1.0	0	<1.0	
	Ipronidazole	30	28	22	<1.0	0	<1.0	
	Ipronidazole - OH (PZOH)	30	28	22	<1.0	0	<1.0	
	Metronidazole-OH (VNZOH)	30	28	22	<1.0	0	<1.0	
	Ternidazole	30	28	22	<1.0	0	<1.0	
	Hydroxy Dimetridazole (HMMNI)	30	28	22	<1.0	0	<1.0	
Other A2 Substances	Chlorpromazine	34	32	33	<0.1	0	<0.1	
	Dapsone	34	32	33	<2.7	0	<2.7	
Total		608	659	397	-	2	-	

Note: *: According to (Commission Regulation (EU) No 37/2010; Regulation (EC) No 396/2005; Commission Regulation (EC) No 1881/2006)

Furthermore, during the reporting period, no residues of insecticides (ivermectin, moxidectin, doramectin and eprinomectin) were found in cow's milk (a total of fifty-three samples were tested for ivermectin and fifty milk samples – for the remaining drugs).

Cow's milk screening results for NSAIDs, corticosteroids and glucocorticoids are presented in Table 3. Thus, in the period from 2020 to 2023, 403 milk samples were tested for the above-mentioned drugs. It should be noted that residual amounts of phenylbutazone, meloxicam, 5-hydroflunexin, tolfenamic acid and prednisone were not found in any sample (Table 3).

Ukrainian cow's milk screening results for organochlorine and organophosphate compounds for 2020-2023 are presented in Table 4. A total of 410 (287 and 123) milk samples were tested for chlorine- and phosphate-containing compounds during the reporting period. Residual amounts of hexachlorobenzene, heptachlor, γ-HCCG, α-HCCG, β-HCCG, dichloro-diphenyl-trichloro-methyl-methane and its metabolites, Sum PCB 28, PCB 52, PCB 101, PCB 138, PCB 153, PCB 180, diazinon, parathion-methyl, malathion were not found in any sample (Table 4).

Table 6 presents the Ukrainian cow's milk screening results for heavy metals, mycotoxins and radionuclides for 2020-2023. Fifty-two milk samples were tested for heavy metals (25 samples for lead, 24 for mercury and 3 for cadmium), but their residual quantity was not found in any sample. In 2020-2023, fifty milk samples were tested for aflatoxin M1, but its residual quantity was not found in any sample. Cesium-137 and

Table 2. Ukrainian cow's milk screening results for antimicrobials for 2020-2023, μg/l.

Drug name	Number of tested samples by year			Detection limit (method)	Number of positive samples	Determined concentration	Maximum residue limit*
	2020-2021	2022	2023				
Benzylpenicillin	29	33	26	<4.97	0	<4.97	4
Amoxicillin	29	33	26	<4.11	0	<4.11	4
Ampicillin	29	33	26	<4.15	0	<4.15	4
Florfenicol	29	33	26	<62.4	0	<62.4	Not permitted
Tetracycline	38	37	26	<109.31 (CCα)	0	<109.31 (CCα)	100
Chlortetracycline	38	37	26	<107.07 (CCα)	0	<107.07 (CCα)	100
Oxytetracycline	38	37	26	<108.09 (CCα)	0	<108.09 (CCα)	100
Doxycycline	38	37	26	<53.72 (CCα)	0	<53.72 (CCα)	Not permitted
Kanamycin	37	33	26	<161.0	0	<161.0	150
Apramycin	37	33	26	<227.0	0	<227.0	Not permitted
Cloxacillin	37	33	26	<31.2 (CCα)	0	<31.2 (CCα)	30
Enrofloxacin	37	33	26	<126.0	0	<126.0	100
Norfloxacin	37	35	26	<12.5	0	<12.5	Not permitted
Ciprofloxacin	37	35	26	<126.8	0	<126.8	100
Flumequine	37	35	26	<56.0	0	<56.0	50
Streptomycin	37	33	26	<232.0	0	<232.0	200
Dihydrostreptomycin	29	33	26	<216.0	0	<216.0	200
Spectinomycin	29	33	26	<226.0	0	<226.0	200
Erythromycin	29	33	26	<45.14	0	<45.14	40
Tylosin	29	33	26	<59.02	0	<59.02	50
Neomycin	29	33	26	<1610.0	0	<1610.0	1500
Gentamicin	29	33	26	<126.0	0	<126.0	100
Lincomycin	29	33	26	<183.0	0	<183.0	150
Colistin	29	33	26	<56.2	0	<56.2	50
Sulfathiazole	29	33	26	<102.9	0	<102.9	100
Sulfadimethoxine	36	33	26	<105.7	0	<105.7	100
Sulfaguanidine	36	37	26	<104.7	0	<104.7	100
Sulfadiazine	36	37	26	<102.9	0	<102.9	100
Sulfamerazine	36	37	26	<110.1	0	<110.1	100
Sulfamethazine (Sulfadimedine)	36	37	26	<102.6	0	<102.6	100
Sulfamethoxypyridazine	36	37	26	<103.8	0	<103.8	100
Sulfamethoxazole	36	37	23	<111.2	0	<111.2	100
Sulfanilamide	36	37	23	<105.3	0	<105.3	100
Trimethoprim	36	37	23	<52.7	0	<52.7	50
Ceftiofur	36	37	23	<102.4	0	<102.4	100
Cefquin	36	37	23	<22.0	0	<22.0	20
Cephalexin	36	37	23	<102.9	0	<102.9	100
Tiamulin	36	37	23	<56.1	0	<56.1	Not permitted
Total	1293	1324	967	-	0	-	-

Note: *: According to (Commission Regulation (EU) No 37/2010; Regulation (EC) No 396/2005; Commission Regulation (EC) No 1881/2006)

Table 3. Ukrainian cow's milk screening results for antiparasitic agents, NSAIDs, corticosteroids and glucocorticoids for 2020-2023, µg/l.

Drug name	Number of tested samples by year			Detection limit (method)	Number of positive samples	Determined concentration	Maximum residue limit*
	2020-2021	2022	2023				
Albendazole	12	12	26	<106.53	0	<106.53	100
Fenbendazole	12	12	26	<10.7	0	<10.7	10
Levomizole	12	12	26	<6.18	0	<6.18	Not permitted
Clorsulon	12	12	26	<17.21	0	<17.21	16
Closantel	12	12	26	<50.39	0	<50.39	45
Mebendazole	12	12	26	<6.68	0	<6.68	Not permitted
Oxyclozanide	12	12	26	<11.47	0	<11.47	10
Rafoxanide	12	12	26	<11.21	0	<11.21	Not permitted
Ivermectin	12	12	29	<12.53	0	<12.53	Not permitted
Moxidectin	12	12	26	<44.69	0	<44.69	40
Doramectin	12	12	26	<17.74	0	<17.74	Not permitted
Eprinomectin	12	12	26	<24.02	0	<24.02	20
Triclabendazole	12	12	26	<12.73	0	<12.73	10
Total	156	156	341	-	0	-	-
Phenylbutazone	12	12	57	<5.11	0	<5.11	Not permitted
Meloxicam	12	12	57	<15.59	0	<15.59	15
5-Hydroflunexin	12	12	57	<40.64	0	<40.64	40
Tolfenamic acid	12	12	57	<51.29	0	<51.29	50
Prednisone	10	12	57	< 6.7(CCα)	0	< 6.7(CCα)	6
Total	58	60	285	-	0	-	-

Note: *: According to (Commission Regulation (EU) No 37/2010; Regulation (EC) No 396/2005; Commission Regulation (EC) No 1881/2006)

strontium-90 were found in the range of 3.0 and 0.6-0.7 µg/l, respectively, which did not exceed the National MRL and LEVEL OF ACTION, a total of sixty-seven milk samples were tested (Table 4).

Discussion

At the beginning of the discussion, I would like to provide data on infectious diseases detected in dairy herds of cattle in parallel. Thus, during 2021-2022, 24301 samples of biological material were tested, 0.4% of them were positive, and the maximum percentage of positive samples was for colibacillosis– 0.25% in relation to the total number of samples, and 6.1% in relation to the samples tested directly for colibacillosis. 0.03% of the total number samples were positive for tuberculosis and streptococcosis each, which amounted to 1.3 and 15.7% in relation to the samples tested directly for these infections. Staphylococcosis was detected in 0.029% of samples, which amounted almost 9.0% of samples tested directly for staphylococcus. Also, an insignificant number of positive samples were positive for Q fever, salmonellosis, listeriosis, and pasteurellosis – 0.02, 0.016, 0.012 and 0.008% respectively (Table 5). That is, bacterial diseases involving antibiotic use were recorded mainly, which probably led to the isolation of positive samples for chloramphenicol.

Since most microorganisms are sensitive to the antibiotic, it acts on gram-positive and Gram-negative rods: *H. influenzae* (including ampicillin-resistant strains), *E. coli*, *Salmonella*, *Shigella*, causative agents of anthrax, brucellosis and plague. It should be noted that due to the high frequency of side effects and the development of resistance of microorganisms, Chloramphenicol is used in a limited way: only for the treatment of severe infections, in which less toxic antibiotics are ineffective (Bayer *et al*., 2017). Chloramphenicol has a toxic effect on the bone marrow of animals and humans. Along with this, in the technical report of the European Food Safety Authority (Brocca and Salvatore, 2022), Chloramphenicol was determinates in milk samples from Lithuania (6 samples out of 239 or 2.51%) and Poland (one sample out of 291 or 0.34%), while in our research this index is 0.85%.

Relative to drugs with a nitro group, a scientific work deserves for attention, in which were published the results of milk monitoring for the nitrofurans content, conducted in Croatia during 2021-2022: out of 497 research samples, such drugs were identified in 11 samples (2.21%) (Varga *et al*., 2023), while according to our data, these drugs were not detected in milk in Ukraine.

Screening research of antibiotics residues in milk in Italy during 2018-2022 showed a low number of positive samples of antibiotics residues: from 408033 samples, residual value was detected at 0.08% of samples. The β-lactam antibiotics were determined most of all (Amoxicillin, Ampicillin, Penicillin G, Cloxacillin, Dicloxacillin, Nafcillin, Oxacillin, Cefalexin, Cefapirin, Cefazolin), and penicillin G was the most common compound (Butovskaya *et al*., 2023).

Regarding antiparasitic drugs in cow's milk, no similar studies from large-scale monitoring or screening were found in the last 5 years, but Polish researchers in 2015, as a result of screening goat and sheep milk and dairy products from the Polish market for the content of albendazole (and metabolites), cambendazole, fenbendazole (and metabolites), flubendazole (and metabolites), mebendazole (and metabolites), oxybendazole, thiabendazole (and metabolites), triclabendazole (and metabolites); macrocyclic lactones: abamectin, doramectin, emamectin, eprinomectin, ivermectin, moxidectin; salicylanilides: clozantel, ioxinil, nitroxinil, oxyclozamide, niclosamide, rafoxanid and others: clorsulon, derquantel, imidocarb, monepantel (and metabolites), morantel, praziquantel, and pyrantel were not detected in any of the 120 samples (Jedziniak *et al*., 2015). The Technical report of the European Food Safety Authority (Brocca and Salvatore, 2022) indicates the presence of 0.09% positive samples for anthelmintics in milk (5 out of 5783 samples): Levamisole, Sum of albendazole: sulphoxide, albendazole sulphone, and albendazole 2-amino sulphone , expressed as albendazole and Sum of extractable residues which may be oxidized to oxfendazole sulphone were determined in milk from Ireland (0.25, 0.51 and 0.25% of samples) and Sum of albendazole: sulphoxide, albendazole sulphone, and albendazole 2-amino sulphone, expressed as albendazole in 0.13% of samples from France. The index of anthelmintic drugs were slightly lower in 2021 (Brocca *et al*., 2023): 0.04% of positive samples for anthelmintics in milk were determined (3 out of 6690 samples): Levamisole was determined in milk from Ireland in 0.49% of samples and Sum of albendazole: sulphoxide, albendazole sulphone, and

Table 4. Ukrainian cow's milk screening results for organochlorine and organophosphate compounds, heavy metals, mycotoxins and radionuclides for 2020-2023, μg/l.

Drug name	Number of tested samples by year			Detection limit (method)	Number of positive samples	Determined concentration	Maximum residue limit*	
	2020-2021	2022	2023					
Organochlorine compounds:	84	98	105				National MRL	EU MRL i LEVEL OF ACTION
Hexachlorobenzene	12	14	15	<1.0	0	<1.0	Not permitted	5
Heptachlor	12	14	15	<1.0	0	<1.0	50	4
γ-HCCG -hexachloran, lindane, gamma isomer	12	14	15	<1.0	0	<1.0	50	10
α-HCCG - α-1,2,3,4,5,6-hexachlorocyclohexane	12	14	15	<1.0	0	<1.0	50	10
β-HCCG - beta-1,2,3,4,5,6-hexachlorocyclohexane	12	14	15	<1.0	0	<1.0	50	10
Dichloro-diphenyl-trichloro-methyl-methane and its metabolites (4,4-DDT, 4,4-DDD, 4,4-DDE)	12	14	15	<1.0	0	<1.0	40	40
Sum PCB 28, PCB 52, PCB 101, PCB 138, PCB 153, PCB 180	12	14	15	<1.0	0	<1.0	50	40
Organophosphate compounds:	36	42	45				National MRL	EU MRL i LEVEL OF ACTION
Diazinon	12	14	15	<1.0	0	<1.0	Not permitted	20
Parathion-methyl	12	14	15	<1.0	0	<1.0	Not permitted	10
Malathion	12	14	15	<1.0	0	<1.0	Not permitted	20
Total	120	140	150	-	0	-	-	
Heavy metals	11	15	26				National MRL i LEVEL OF ACTION	EU MRL
Lead	3	8	14	<10.0	0	<10.0	20	20
Mercury	5	7	12	<5.0	0	<5.0	10	10
Cadmium	3	0	0	<5.0	0	<5.0	10	Not permitted
Aflatoxin M1	12	12	26	<0.05	0	<0.05	0.05	0.05
Radionuclides	80	24	30				National MRL	EU MRL i LEVEL OF ACTION
Cesium -137	40	12	15	<3.0	0	3.0±0,02	100	Not permitted
Strontium -90	40	12	15	<0.6	0	0.6±0,02 0.7±0,03	20	Not permitted

Note: *: According to (Commission Regulation (EU) No 37/2010; Regulation (EC) No 396/2005; Commission Regulation (EC) No 1881/2006) and National MRL (SanPiN 8.8.1.2.3.4-000-2001; SSU 4273–2015; Order of the Ministry of Health of Ukraine…)

albendazole 2-amino sulphone, expressed as albendazole – in 2.27% of samples from Italy.

NSAIDs were detected in 0.41% of milk samples (21 out of 5165) from six EU countries (Brocca and Salvatore, 2022) in 2020: they were mainly Diclofen (Diclofenac) – Belgium – 1.64% of positive samples, Croatia – 2.63%, Germany – 0.7%, Malta – 0.57%, Slovenia – 0.49% of milk samples and Salicylic acid – Belgium – 3.28% positive samples, Germany – 1.56% and the Netherlands – 0, 3%, while corticosteroids and glucocorticoids were not detected in cow's milk. However, in 2021, this indicator increased to 0.47% (27 out of 5698 milk samples) – NSAIDs (Acetaminophen (Paracetamol), Diclofen (Diclofenac), Salicylic acid and Ketoprofen) were detected in milk from 13 EU countries: from 0.13% in Germany to 14.71% in Belgium (Brocca *et al*., 2023).

If, according to (Brocca *et al*., 2023), in 2021, Organochlorinated and Organophosphate compounds were not detected in cow's milk obtained from EU farms, while in 2020 (Brocca and Salvatore, 2022) in 0.17% of milk samples (3 of 1793) were determined organochlorine compounds, including PCBs.

According to the monitoring data of organochlorine residues in raw bovine milk in the west Delta area, Egypt the obtained results revealed that DDT, dieldrin, endrin, and lindane were detected in Alexandria, Behera, and Matrouh at incidence levels (22.7%, 30.7%, and 10.0%), (20.0%, 20.0% and 16.0%), (9.33%, 13.3% and 16.0%), and (12.0%, 10.7% and 14%) with mean values of 232.2±163.6, 156.4±134.6 and 100.4±85.9; 91.3±61.2, 95.3±59.8 and 57.6±3.33; 15.7±3.86, 15.1±3.96 and 20.1±7.33; 33.7±10.6, 36.9±5.51 and 52.2±21.8 ng/g fat, respectively (El-Makarem and Abushaala, 2023). The concentration profile of organochlorine pesticides (18 compounds) in cow`s milk in eight major districts of Punjab, Pakistan was also evaluated. Their total content in milk samples ranged from 14.64 to 77.93 ng ml-1. The overall picture of the average concentration of OCPs in cow's milk showed that hexachlorocyclohexane (HCH) predominated, followed by heptachlor and dichlorodiphenyltrichloroethane (DDT), but in addition, ∑HCH, ∑DDT and ∑heptachlor did not exceed the maximum residue levels established for milk (Sana *et al*., 2021). Studies of residues amount of organophosphate pesticides in milk samples in Sudan showed the presence of 2 pesticides of the organophosphorus group (dimethoate and chlorpyrifos in amounts from 4 to 92% of samples, depending on the sampling area), but all positive samples were below the maximum residue level (Sara *et al*., 2019).

Heavy metals were not detected in cow's milk samples from the EU in 2020 and 2021 according to EFSA reports (Brocca and Salvatore, 2022; Brocca *et al*.,2023). But a high level of Pb (3.80±0.42 mg/l) was determined in samples of raw cow's milk taken from a local producer in the Nitra region (Slovakia), compared to the permissible limit for milk accord-

Table 5. Screening results for infectious diseases in Ukraine for 2021-2022.

Disease	2021		2022	
	Number of tests	Positive results	Number of tests	Positive results
Colibacillosis	894	51	88	9
Campylobacteriosis	436	0	579	0
Brucellosis	126	0	51	0
Leptospirosis	11	0	6	0
Listeriosis	3824	3	42	0
Pasteurellosis	106	1	74	1
Salmonellosis	370	4	173	0
Anthrax	192	0	156	0
Tuberculosis	474	8	148	0
Staphylococcosis	66	0	12	7
Streptococcosis	39	1	12	7
Chlamydiosis	6223	0	3295	0
Foot-and-mouth disease	6722	0	0	0
Q fever	120	0	62	5
Total	19603	68	4698	29

ing to Slovak legislation (0.02 mg/l) (Capcarova *et al*., 2019). In milk from 16 livestock farms in Spain, maximum levels of potentially toxic elements were significantly lower than in soil or feed: 74.1, 16.1, 0.12, 0.28 and 2.7 μg kg^{-1} for chromium, arsenic , cadmium, mercury and lead, respectively, and none of the milk samples exceeded the permissible content limits established by the EU (Forcada *et al*., 2023). Mycotoxins (Aflatoxin M1) were determined in 0.26% of milk samples (4 out of 1568) from three EU countries (Brocca and Salvatore, 2022) in 2020: from Bulgaria – in 10% of samples, Croatia – 3.03% and from Finland – 1.15%. This index was slightly higher in 2021 – 0.27% (6 out of 2212), Aflatoxin M1 was detected in milk from Croatia (2.82%) and Greece – 4.49% (Brocca *et al*., 2023). In the study (Ferrari *et al*., 2023), a total of 95882 samples of whole raw milk, collected in northern Italy between 2013 and 2021, were evaluated for presence of AFM1, only 667 milk samples (0.7%) showed AFM1 values higher than the EU threshold limit of 50 ng/L. A total of 390 samples (0.4%) showed values between 40 and 50 ng/L, thus requiring corrective action despite not surpassing the regulatory threshold.

Scientists from the Netherlands measured radioactivity in 756 samples of cow's and 17 goat's milk, but the limits of radiocesium (sum of 134Cs and 137Cs) in milk and milk products (370 $Bq.kg^{-1}$) were not exceeded (Tanzi and Knetsch, 2021).

Conclusion

In the period of 2020-2023 7138 samples of cow's milk from native dairy enterprises from 25 regions of Ukraine were screened for the content of various dangerous substances and compounds from groups A (Substances having anabolic effect and unauthorized substances) and B (Veterinary drugs and contaminants) which are declared in Directive 96/23/EC. It was established that the milk of cows from Ukraine, obtained in the period 2020-2023, despite the COVID-19 pandemic and martial law, meets current national standards and is not inferior in terms of quality and safety to EU indicators. Among the inconsistent results, it is worth highlighting the presence of Chloramphenicol in 0.85% of milk samples out of 234 tested for its content, which was 0.03% of the total number of samples, while the content of other investigated drugs and substances was below of the methods detection limit.

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Conflict of interest

The authors declare that they have no potential conflict of interest with respect to the authorship and/or publication of this article.

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