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Efficiency of using levamisole-based anthelmintics

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Abstract. Animal parasitic diseases cause major losses to the livestock industry and require constant monitoring and control. The purpose of this study was to monitor the livestock (calves, goats, sheep, pigs, dogs, chickens) for the presence of helminthic pathogens, to determine the therapeutic efficacy of levamisole-based preparations and the general toxicity of meat of experimental animals using the *Colpoda steinii* test culture. In 2020-2022, a considerable spread of invasive animal diseases was

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detected in the Kharkiv region of Ukraine. In a study of 3,500 calves, 1,000 (28.6%) were found to be persistently infected with nematodes with an intensity of 25.0-150.0 worm eggs per 1 g of faeces. In goats, the intensity of endoparasite infection ranged within 10.0-15.0 worm eggs per 1 g of faeces, while in sheep this figure reached 25.0 worm eggs per 1 g of faeces. In the study of faeces from pigs, 800 (34.8%) samples revealed the presence of helminth eggs, while mono-infestation was detected in 300 samples (37.5%). In the study of canine faeces, 10 (66.7%) positive samples were found. When examining the manure from chickens, 200 (44.4%) positive samples revealed the presence of helminth eggs. The use of levamisole dosage forms can reduce the extent of infection in animals by 50% as early as on Day 5. No worm eggs were detected in the faeces of animals from Day 14 to Day 30 of observation, and therefore the extensional efficacy of the studied products under modern conditions is 100%. Meat obtained from farm animals (pigs, calves, sheep) treated with levamisole-based preparations shows signs of general toxicity within 5-9 days after the use of the products: 5 days for pigs and 9 days for calves and sheep. At the same time, meat obtained from poultry (chickens) treated with levamisole-based preparations shows signs of general toxicity within 2 days after the end of the treatment course

Keywords: levamisole; endoparasites; helminth eggs; antiparasitic agent; extensive and intensive invasion; meat; toxicity

INTRODUCTION

Tens of thousands of species on the planet have adapted to a parasitic lifestyle. It is difficult to name a species of animal that does not have helminths. Helminthiasis is one of the most common diseases of cattle, pigs, poultry, and exotic poultry, and domestic animals (Paliy *et al.*, 2019; Galat *et al.*, 2019; Bohach *et al.*, 2023). According to J.W. Lewis (2016), the effect of parasites on the host depends on the intensity of infection, age, host resistance, conditions of housing, feeding, and a series of environmental factors. M. Rashid *et al.* (2019) and S. Ola-Fadunsin *et al.* (2020) show a decrease in the productivity and quality of livestock products and large economic losses caused by parasitic animal diseases worldwide.

S.A. Nixon *et al.* (2020) note that the type of infectious agent and the number of eggs and larvae found in animal excrement are of significant importance. Prevention and control of animal diseases has always been one of the principal and crucial areas of work for any veterinarian. According to R.W. Avramenko *et al.* (2017), the effectiveness of antiparasitic measures directly depends on the availability of highly effective veterinary medicines. H.R. Vineer *et al.* (2020) and J. Charlier *et al.* (2023) note that the issue of parasite resistance to anthelmintics is becoming a major issue in veterinary medicine and poses a serious threat to animal welfare. In veterinary medicine, C. Chartier *et al.* (2020) are testing anthelmintics with different ratios of active ingredients, but the number of infected animals is constantly growing.

Residual content of veterinary preparations in animal products can have a negative impact on human health. According to J.T. Campillo *et al.* (2022), levamisole contributes to the development of vasculitis, neuropathy, agranulocytosis, and leukoencephalopathy in humans. It was because of the elevated risk of these side effects that levamisole was withdrawn from the US and Canadian human medication markets in 2000 and 2003, respectively. Although the probability of acute human intoxication from levamisole residues and its metabolites in meat products has been proven to be low, due to the widespread use of the preparation in animal treatment, concerns about their content persist. To ensure the safety of slaughter products for human consumption, monitoring protocols have been developed for veterinary preparations, including anthelmintics, which include the establishment of maximum residue limits (MRLs).

The purpose of this study was to determine the endoparasite prevalence in animals in the Kharkiv region (Ukraine), to determine the effectiveness of helminthic infections treatment with preparations containing levamisole and the general toxicity of meat by biotesting obtained from animals treated with levamisole.

MATERIALS AND METHODS

The study was conducted within the framework of the state scientific theme of the National Research Centre "Institute of Experimental and Clinical Veterinary Medicine" 34.01.02.02 F "Investigation of the role of arthropods in the spread of pathogens of parasitic and infectious diseases and development of a strategy to combat them" No. DR 0121U108356 (2020–2022) and the initiative research work of Odesa State Agrarian University "Ensuring animal welfare, food safety, and quality in the context of European integration" No. 0123U103523 (2023-2028).

Two preparations from different manufacturers containing the active ingredient levamisole were used in the trials: preparation No. 1, Levamisole Plus 10% (solution for injection); preparation No. 2, Levamisole 10%. The preparations were administered individually, orally, subcutaneously, or intramuscularly in the following doses: cattle, small cattle, pigs – 0.75 ml per

10 kg of body weight; dogs – 0.75 ml per 10 kg of body weight, once, orally; poultry – 1.0 ml per 250 ml of drinking water for three consecutive days orally.

The experiments were carried out in the laboratory of veterinary sanitation and parasitology of the National Scientific Centre "Institute of Experimental and Clinical Veterinary Medicine", the Multidisciplinary Laboratory of Veterinary Medicine of Odesa State Agrarian University and in livestock farms of various forms of ownership in the Kharkiv Oblast of Ukraine in 2020-2023. Clinical trials of preparations on animals to investigate their therapeutic effect were conducted according to the following scheme:

1) clinical examination of animals, preliminary diagnosis, faecal sampling for laboratory testing, and ongoing clinical monitoring of the physiological state of experimental animals;

2) microscopic examination of samples to determine the pathogens of helminthic diseases in the biological material, their identification, and determination of the extent of infections in animals;

3) administration of preparations, individually, keeping animals, taking faecal samples for laboratory testing 5, 10, 15, and 30 days after the last preparation administration; determination of the preparation efficacy.

Total number of animals studied: black-and-white dairy calves aged 4-12 months (n = 3,500), goats (n = 200) and sheep (n = 300) aged 1-5 years, pigs (n = 2,300: 50 sows, 10 boars, and 1,700 piglets aged 3-4 months), non-pedigree dogs (n = 15) aged 6 months to 7 years, chickens (n = 450) of the Leghorn breed.

Experimental group I – animals treated with preparation No. 1 "LEVAMISOL-plus 10% (solution for injection)": calves (n = 500), goats (n =м60), sheep (n = 50), pigs (n = 400), dogs (n = 5), chickens (n = 100);

Experimental group II – animals treated with preparation No. 2 "Levamisole 10%": calves (n = 500), goats (n = 60), sheep (n = 50), pigs (n = 400), dogs (n = 5), chickens (n = 100).

Experimental group III (control) – clinically healthy animals without the use of levamisole-based preparations: calves (n = 2,500), goats (n = 80), sheep (n = 200), pigs (n = 1,500), dogs (n = 5), chickens (n = 250).

Experimental animals treated: calves (n = 1,000), goats (n = 120), sheep (n = 100), pigs (n = 800), dogs (n = 10), chickens (n = 200). According to the objectives, the study was conducted using visual and microscopic methods (Robinson & Dalton, 2009; Collender *et al.*, 2015). The study carried out in vivo diagnostics of helminth infections and determined the number of helminth eggs. The intensity of infection was determined by counting the number of worm eggs per 1 g of faeces.

At 5, 10, 15, and 30 days after treatment, the results of the study were recorded based on examinations of treated animals, detection of worm eggs in faecal samples, determination of the extent of invasion after treatment and the extensefficacy of the preparation. Faecal samples were examined for the presence of helminth eggs using the native smear method, the Fülleborn flotation method, and the Berman method (Bahur & Zgozinska, 2015; Dakhno, 2023) using a light microscope at a magnification of ×100. The detected worm eggs and larvae were examined under magnification (×400) for identification. The extent of the infestation was determined according to the following formula:

$$IE = \frac{x}{y} \times 100, \quad (1)$$

where *IE* is the invasion extensiveness; *x* is the number of faecal samples in which worm eggs were detected; *y* is the total number of faecal samples; 100 is the conversion factor to percentage.

The general toxicity of meat of animals treated with levamisole was studied by the author's biological express method using the infusoria *Colpoda steinii* as a test object (The method of determining the toxicity of the meat of slaughtered animals: Patent No. 149685, Ukraine, 2022; Gorobey *et al.*, 2022)

The total number of meat samples from the experimental animals: calves (n = 54), sheep (n = 54), pigs (n = 45), chickens (n = 45).

Experimental group I – meat of animals treated with preparation No. 1 "LEVAMIZOL-plus 10% (solution for injection)": calves (n = 18), sheep (n = 18), pigs (n = 15), chickens (n = 15);

Experimental group II – meat of animals for the treatment of helminthiasis where preparation No. 2 "Levamisole 10%" was used: calves (n = 18), sheep (n = 18), pigs (n = 15), chickens (n = 15).

Experimental group III (control) – meat of clinically healthy animals without the use of levamisol-based preparations: calves (n = 18), sheep (n = 18), pigs (n = 15), chickens (n = 15).

The general toxicity study was conducted for 11 days with an interval of 1 day. To determine the toxicity, a test culture of *Colpoda steinii* was prepared by adding 2 cm^3 of culture medium to a vial of dry culture and placing it in a thermostat for 24 hours at +26…+28°C. A sample of meat weighing 10 g was taken, the sample was extracted with aqueous acetone in a volume of 10 cm^3, shaken for 20 minutes, and filtered. 0.5 cm^3 of filtrate was collected and 60 cm^3 of Lozin-Lozinsky solution was added. Subsequently, 2 cm^3 of the obtained acetone extract solution was added to a vial with the prepared test culture of *Colpoda steinii* infusoria, placed in a thermostat for 1 hour at +26…+28°C. After thermostatting, the working mixture was examined under a microscope at a magnification of x80-120 to determine the condition and behaviour of the test culture and to count the percentage of live and dead infusoria (Table 1).

***Table 1**. Criteria for the assessment of general toxicity*

Condition and behaviour of the test culture of the infusoria *Colpoda steinii*	Degree of toxicity			
	Non-toxic	Slightly toxic	Toxic	Highly toxic
Live (active/motile) infusoria, %	90-100	80-85	5-10	0
Unnatural movements, %	0-2	3-5	3-5	0
Growth inhibition, %	0-2	3-5	3-5	0
Pathological forms, %	0-2	3-5	3-5	0
Dead infusoria, %	0-5	5-10	70-90	100

***Source:** developed and patented by the authors of this study (The method of determining the toxicity of the meat of slaughtered animals: Patent No. 149685, Ukraine, 2022)*

The experiments conducted on animals follow the requirements of DSTU ISO/IEC 17025:2005 (2006), the Regulation on the Procedure for Conducting Experiments and Experiments on Animals by Scientific Institutions (Law of Ukraine No. 249, 2012), the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (European convention..., 1986) and international bioethical standards (materials of the IV European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Purposes (Council Directive 86/609/EEC, 1986).

RESULTS AND DISCUSSION

Determination of the extent of animal endoparasite infestation. As a result of the clinical examination of calves, animals were found to be underweight, emaciated, with dull, tousled hair, signs of digestive disorders – bloating, discharge of liquid faeces.As a result of coprological examination of faeces from calves, eggs of various helminths were found (Table 2).

In the study of 3,500 calves, 1,000 (28.6%) of them were found to be persistently infested with endoparasites of different species composition. In calves, mono-infestations with nematodes were observed with an intensity of 25.0-150.0 worm eggs per 1 g of faeces.

During the examination of small cattle (sheep, goats), clinical signs of digestive disorders were found – abdominal distention, unformed faeces. Faeces from small cattle (sheep, goats) were examined and worm eggs were found (Table 3).

***Table 2**. Infestation of calves with helminths (M ± m, n = 3,500)*

Type of parasite	Samples, pcs.	Invasion extensiveness, %	Invasion intensity
Haemonchus spp.	400	11.4	150.0 ± 13.5
Nematodirus spp.	200	5.8	25.0 ± 5.5
Ostertagia spp.	400	11.4	25.0 ± 1.5

***Source:** developed by the authors of this study*

***Table 3**. Infestation of goats (M ± m, n = 200) and sheep (M ± m, n = 300) with helminths*

Type of parasite	Samples, pcs.	Invasion extensiveness, %	Invasion intensity
goats			
Trichostrongylus spp.	40	20	15.0 ± 1.5
Nematodirus spp.	40	20	15.0 ± 1.5
Cooperia spp.	40	20	10.0 ± 0.5
sheep			
Haemonchus spp.	40	13.3	15.0 ± 0.5
Nematodirus spp.	20	6.7	10.0 ± 1.5
Ostertagia spp.	40	13.3	25.0 ± 1.5

***Source:** developed by the authors of this study*

At the time of the survey, the extent of infection among goats was higher than in sheep, at 60% and 33.3%, respectively. Mono-invasions were detected in animals with varying intensity. Thus, in goats, the intensity of endoparasite infection ranged within 10.0-15.0 helminth eggs per 1 g of faeces, while in sheep this figure reached 25.0 helminth eggs per 1 g of faeces. During the examination of pigs with clinical manifestations of digestive disorders (liquid faeces), nematode eggs were found in faeces (Table 4).

Table 4. *Infection of pigs with helminths (M ± m, n = 2,300)*

Type of parasite	Samples, pcs.	Invasion extensiveness, %	Invasion intensity
Ascaris suum	400	17.4	35.0±5.5
Oesophagostomum spp.	200	8.7	15.0±1.5
Strongyloides ransomi	400	17.4	45.0±3.5

Source: *developed by the authors of this study*

In the study of faeces from pigs, 800 (34.8%) samples revealed the presence of helminth eggs, while mono-infestation was detected in 300 samples, which is 37.5%. Twenty sows were found to be infected with *Ascaris suum*, and boars – with *Oesophagostomum* spp. The presence of a mixed invasion was detected in piglets – 62.5%. Dogs with clinical manifestations of digestive disorders (distorted appetite, liquid faeces) were also examined. Faecal samples were collected from the animals for parasitological studies (Table 5).

Table 5. *Infection of dogs with helminths (M ± m, n = 15)*

Type of parasite	Samples, pcs.	Invasion extensiveness, %	Invasion intensity
Toxocara canis	4	26.7	35.0±3.5
Toxascaris leonina	6	26.7	15.0±1.5
Ancylostoma spp.	2	13.3	25.0±3.5
Uncinaria spp.	2	13.3	15.0±1.5

Source: *developed by the authors of this study*

The study revealed 10 (66.7%) positive samples, with monoinvasion detected in 8 samples, which is 80%. Eggs of *Toxocara canis* were detected in two dogs aged 4 years, and Toxascaris leonina was indicated in six animals aged 3-5 years. Two dogs were also found to be infected with parasites *Toxocara canis, Ancylostoma* spp., and *Uncinaria* spp. According to the results of the studies, the highest intensity of *Toxocara canis* infection was 35.0 worm eggs per 1 g of faeces, and the lowest was *Toxascaris leonina* and *Uncinaria* spp. – 15.0 worm eggs per 1 g of faeces each. In the study of chicken manure, in 200 (44.4%) positive samples, monoinfestation of *Ascaridia galli* was detected in 100 (50%) chickens, monoinfestation of *Heterakis gallinarium* – in 50 chickens (25%), and *Capillaria* spp. – in 50 (25%) chickens. The intensity of infection was highest for *Ascaridia galli* (45 eggs per 1 g of faeces), and lowest – for *Capillaria* spp. (10 eggs per 1 g of faeces) (Table 6).

Table 6. *Helminth infestation in chickens (M ± m, n = 450)*

Type of parasite	Samples, pcs.	Invasion extensiveness, %	Invasion intensity
Ascaridia galli	100	22.2	45.0±1.5
Heterakis gallinarium	50	11.1	15.0±1.5
Capillaria spp.	50	11.1	10.0±3.5

Source: *developed by the authors of this study*

Determination of the effectiveness of treatment of helminth infections in animals with preparations containing levamisole. After identifying animals infected with various types of helminths, they were given experimental levamisole preparations for therapeutic purposes. At the first stage, the therapeutic efficacy of the preparations in nematode infections in ruminants was determined (Table 7).

Table 7. *Study of the therapeutic efficacy of levamisole preparations in ruminants*

Type of helminths	Before treatment		After treatment							
	IE, %	II, avg	Day 5		Day 10		Day 20		Day 30	
			IE, %	II	IE, %	II	IE, %	II	IE, %	II
Calves (n=500), preparation No. 1										
Haemonchus spp.	100	150	50	65	50	5	0	0	0	0
Nematodirus spp.	100	25	0	0	0	0	0	0	0	0
Ostertagia spp.	100	25	50	2	0	0	0	0	0	0

Table 7. Continued

Type of helminths	Before treatment		After treatment							
	IE, %	II, avg	Day 5		Day 10		Day 20		Day 30	
			IE, %	II	IE, %	II	IE, %	II	IE, %	II
Calves (n = 500), preparation No. 2										
Haemonchus spp.	100	132	50	45	50	3	0	0	0	0
Nematodirus spp.	100	30	0	0	0	0	0	0	0	0
Ostertagia spp.	100	23	50	2	0	0	0	0	0	0
Goats (n = 60), preparation No. 1										
Trichostrongylus spp.	100	15	50	7	0	0	0	0	0	0
Nematodirus spp.	100	14	50	8	0	0	0	0	0	0
Cooperia spp.	100	17	50	7	0	0	0	0	0	0
Goats (n = 60), preparation No. 2										
Trichostrongylus spp.	100	17	50	8	0	0	0	0	0	0
Nematodirus spp.	100	16	50	8	0	0	0	0	0	0
Cooperia spp.	100	17	50	8	0	0	0	0	0	0
Sheep (n = 50), preparation No. 1										
Haemonchus spp.	100	15	50	8	0	0	0	0	0	0
Nematodirus spp.	100	10	0	0	0	0	0	0	0	0
Ostertagia spp.	100	25	50	12	0	0	0	0	0	0
Sheep (n = 50), preparation No. 2										
Haemonchus spp.	100	14	50	10	0	0	0	0	0	0
Nematodirus spp.	100	8	0	0	0	0	0	0	0	0
Ostertagia spp.	100	23	50	11	0	0	0	0	0	0

Note: *IE – invasion extensiveness; II – invasion intensity*
Source: *developed by the authors of this study*

After the use of antiparasitic preparations, the presence of *Haemonchus* spp. eggs in the faeces of calves was detected up to 10 days. Therewith, after the administration of the preparations, the extent of *Haemonchus* spp. and *Ostertagia* spp. infestation in calves decreased by 50% as early as on Day 5. The average infestation intensity decreased by 43.3% and 92.0%, respectively, compared to the average infestation intensity before treatment. No worm eggs were found in the faeces of animals from Day 14 to Day 30 of observation, and therefore the extensional effectiveness of the products is 100%. After the administration of the preparations in goats and sheep, the extent of worm infection decreased by 50% on Day 5. The passage of mature worms was observed up to Day 3. No worm eggs were found in the faeces of animals from Day 10 to Day 30 of observation, and therefore the extensefficacy of the preparations is 100%. After the use of antiparasitic preparations in ruminants, no increased individual sensitivity was observed. Levamisole was administered individually to infested pigs (Table 8).

Table 8*. Study of the therapeutic efficacy of levamisole preparations in pigs (n = 800)*

Type of helminths	Before treatment		After treatment							
	IE, %	II, avg	Day 5		Day 10		Day 20		Day 30	
			IE, %	II	IE, %	II	IE, %	II	IE, %	II
Preparation No. 1 (n = 400)										
Ascaris suum	100	32	50	45	50	5	0	0	0	0
Oesophagostomum spp.	100	12	0	0	0	0	0	0	0	0
Strongyloides ransomi	100	40	50	48	0	0	0	0	0	0
Preparation No. 2 (n = 400)										
Ascaris suum	100	30	50	43	50	6	0	0	0	0
Oesophagostomum spp.	100	14	0	0	0	0	0	0	0	0
Strongyloides ransomi	100	43	50	49	0	0	0	0	0	0

Note: *IE – invasion extensiveness; II – invasion intensity*
Source: *developed by the authors of this study*

No individual hypersensitivity was observed in pigs after administration of levamisole preparations. Only *Ascaris suum* eggs were detected *in* the faeces of pigs up to Day 10, and an increase in the egg count in the faeces was observed on Day 5. After the administration of the preparations, the extent of worm infection in pigs decreased by 50% on Day 5. No worm eggs were found in the faeces of animals from Day 14 to Day 30 of observation, and therefore the extensional effectiveness of the products is 100%. At the next stage, the infected dogs were treated with levamisole (Table 9).

***Table 9**. Study of the therapeutic efficacy of levamisole preparations in dogs (n = 10)*

Type of helminths	Before treatment		After treatment							
	IE, %	II, avg	Day 5		Day 10		Day 20		Day 30	
			IE, %	II	IE, %	II	IE, %	II	IE, %	II
Preparation No. 1 (n = 5)										
Toxocara canis	100	35	50	45	50	5	0	0	0	0
Toxascaris leonina	100	16	0	0	0	0	0	0	0	0
Ancylostoma spp.	100	25	0	0	0	0	0	0	0	0
Uncinaria spp.	100	15	0	0	0	0	0	0	0	0
Preparation No. 2 (n = 5)										
Toxocara canis	100	37	50	43	50	6	0	0	0	0
Toxascaris leonina	100	14	0	0	0	0	0	0	0	0
Ancylostoma spp.	100	23	0	0	0	0	0	0	0	0
Uncinaria spp.	100	15	0	0	0	0	0	0	0	0

***Note:** IE – invasion extensiveness; II – invasion intensity*
***Source:** developed by the authors of this study*

No hypersensitivity was observed in dogs after individual oral administration of levamisole preparations. Passage of mature worms in faeces was observed up to Day 3. Until Day 10, only *Toxocara canis* eggs were detected in the faeces of dogs, and an increase in the number of eggs of this helminth species in the faeces was observed on Day 5. After the administration of the preparations, the extent of worm infection in dogs decreased by 50% on Day 5. No worm eggs were found in the faeces of animals from Day 14 to Day 30 of observation, and therefore the extensional effectiveness of the products is 100%. The efficacy of levamisole preparations was also determined on infected chickens (Table 10).

***Table 10**. Study of the therapeutic efficacy of levamisole preparations in chickens (n = 200)*

Type of helminths	Before treatment		After treatment							
	IE, %	II, avg	Day 5		Day 10		Day 20		Day 30	
			IE, %	II	IE, %	II	IE, %	II	IE, %	II
Preparation No. 1 (n=100)										
Ascaridia galli	100	44	50	45	0	0	0	0	0	0
Heterakis gallinarium	100	16	0	0	0	0	0	0	0	0
Capillaria spp.	100	13	50	8	50	3	0	0	0	0
Preparation No. 2 (n=100)										
Ascaridia galli	100	46	50	43	0	0	0	0	0	0
Heterakis gallinarium	100	14	0	0	0	0	0	0	0	0
Capillaria spp.	100	11	50	8	50	3	0	0	0	0

***Note:** IE – invasion extensiveness; II – invasion intensity*
***Source:** developed by the authors of this study*

No individual hypersensitivity was observed in chickens after oral administration with water. The passage of mature worms was observed from Day 3 to 5. An increase in the count of *Ascaridia galli* eggs in the litter was observed up to Day 5. *Capillaria* spp. eggs were *detected* in the poultry manure up to Day 10, indicating the need for repeated use of the preparation. After the application of the preparations, the extent of worm infection in chickens decreased by 50% on Day 5. From Day 14 to Day 30 of observation, no worm eggs

were detected in the poultry manure, and therefore the extensional effectiveness of the products is 100% with two-time application.

Thus, the use of levamisole dosage forms in farm animals (subcutaneously or intramuscularly), carnivores and poultry (orally) on Day 5 of use reduces the intensity of infection by 50%. The highest extenseffica cy (100%) of the preparations under study was recorded on Day 14 of treatment. No increased individual sensitivity to the test preparations was recorded in domestic animals and pets after the use of levamisole-based antiparasitic preparations for 30 days.

Determination of the toxicity of meat, obtained from animals treated with levamisole, using the test culture Colpoda steinii. During the study of the general toxicity of meat of calves and sheep treated with levamisole, on Days 1 and 3 of the study, toxicity of meat of animals of both experimental groups was detected. On Days 5, 7, and 9 after the application of the experimental preparations, mild toxicity of veal and lamb meat was detected, and on Day 11 no signs of toxicity were found in the meat. Toxicity was detected in meat from pigs treated with levamisole on Day 1 of the study in both experimental groups. On Days 3 and 5 of the study, pork meat showed mild toxicity, while on Days 7 and 9 after the use of the test preparations, the meat showed no signs of toxicity. In contrast to pork meat, meat obtained from chickens treated with levamisole showed mild toxicity in both experimental groups on Day 1 of the study, while no signs of toxicity were detected on Days 3 and 5 of the study. The study of the general toxicity of meat revealed the absence of toxicity in the meat of animals of the III experimental group (control) (Table 11).

***Table 11**. Results of the study of the general toxicity of meat of farm animals and poultry treated with levamisole-based preparations*

Type of processing	Degree of toxicity on the corresponding day of the experiment					
	Day 1	Day 3	Day 5	Day 7	Day 9	Day 11
Calves (n = 54)						
Group I	toxic	toxic	slightly toxic	slightly toxic	slightly toxic	non-toxic
Group II	toxic	toxic	slightly toxic	slightly toxic	slightly toxic	non-toxic
Group III	non-toxic	non-toxic	non-toxic	non-toxic	non-toxic	non-toxic
Sheep (n = 54)						
Group I	toxic	toxic	slightly toxic	slightly toxic	non-toxic	non-toxic
Group II	toxic	toxic	slightly toxic	slightly toxic	non-toxic	non-toxic
Group III	non-toxic	non-toxic	non-toxic	non-toxic	non-toxic	non-toxic
Pigs (n = 45)						
Group I	toxic	slightly toxic	slightly toxic	non-toxic	non-toxic	experiment stopped
Group II	toxic	slightly toxic	slightly toxic	non-toxic	non-toxic	experiment stopped
Group III	non-toxic	non-toxic	non-toxic	non-toxic	non-toxic	experiment stopped
Chickens (n = 45)						
Group I	slightly toxic	non-toxic	non-toxic	experiment stopped		
Group II	slightly toxic	non-toxic	non-toxic	experiment stopped		
Group III	non-toxic	non-toxic	non-toxic	experiment stopped		

***Source:** developed by the authors of this study*

Thus, the results of the general toxicity studies indicate the danger of animal meat after treatment with experimental preparations No. 1 and No. 2. Slaughter of animals for meat is possible on Day 11, and poultry – on Day 3 after the use of preparations in experimental therapeutic doses. Modern antiparasitic preparations are used in the veterinary practice of veterinarians in various forms and have different active substances and excipients. However, the issue of acquired resistance of parasites to anthelmintic preparations poses a serious threat to animal welfare and is manifested primarily by a decrease in animal growth and productivity.

According to J. Charlier *et al*. (2023), sheep/goat nematodes are highly resistant to imidazothiazoles (levamisole), providing high therapeutic efficacy. H. Mohseni *et al*. (2019) investigated the therapeutic efficacy of levamisole (7.5 mg/kg) and albendazole (7.5 mg/kg) against gastrointestinal worms in sheep and found an average efficacy of 44% and 46%, respectively. The determined efficacy indices obtained in the study demonstrate low efficiency, specifically, of levamisole, against gastrointestinal worms in sheep. E.D. van Asselt *et al*. (2018), I. Bagulo *et al*. (2023), studying the effectiveness of different groups of anthelmintic preparations (levamisole at a dose of 0.5 ml/20 kg, albendazole 2.5% at a dose of 2 ml/10 kg, ivermectin 1% at a dose of 1 ml/50 kg) against strongyloidiasis in sheep, prove the high efficiency of levamisole – 95.4%, compared to albendazole (86.2%) and ivermectin (89.8%).

The findings of A.V. Potârniche *et al*. (2021) and M. Mickiewicz *et al*. (2021) suggest the spread of anthelmintic resistance of gastrointestinal nematodes

of goats in Romania and Poland to benzimidazoles and macrocyclic lactones and prove their sensitivity exclusively to levamisole, which stopped the development of helminth larvae by 87-100%. Investigating the efficacy of treatment of chickens infected with gastrointestinal nematodes, S.A. Soudkolaei *et al*. (2021) used levamisole at a dose of 16 mg/kg and fenbendazole at a dose of 5 mg/kg for 3 days and proved the efficacy of both anthelmintics. However, the findings of the study showed that fenbendazole (83.7%) was a better and more efficacious deworming agent than levamisole (71.8%).

T. Feyera *et al*. (2021) evaluated the anthelmintic efficacy of levamisole (28 mg/kg), piperazine (100 mg/kg), and fenbendazole (10 mg/kg) against a field strain of *A. galli*, recovered after treatment of poultry with levamisole. It was found that the efficacy of oral administration of levamisole was 99.1%, which was higher than that of other anthelmintics (piperazine – 96.3%, fenbendazole – 97.2%). A. Atta *et al*. (2022) found that the therapeutic level of levamisole persists in the body of animals for 6…9 hours.

When studying the residual content of levamisole in the muscle tissues of laying hens using Nilverm 7.5% at a dose of 20 mg/kg, B. Solomun Kolanović *et al*. (2019) found maximum concentrations of 78.0 μg/kg in the pectoralis muscle and 70.7 μg/kg in the thigh muscle on the first day after preparation administration. Subsequently, a gradual decrease in the residual content of levamisole was observed and the half-life was 3.5 and 3.4 days, respectively, while the period of complete elimination was 14.5 and 13.0 days. P. Cascardo *et al*. (2021) investigated the timing of levamisole residues elimination from the tissues of animals treated with levamisole (10% solution per os at a dose of 10 mg/kg body weight for cattle, sheep, goats, and pigs, and 20 mg/kg for chickens) to a safe level. It was found that in poultry after 3 days, in pigs after 7 days, and in cattle, sheep, and goats after 14 days after treatment, the preparation residues in muscle tissues were below the established limit value.

CONCLUSIONS

It was found that nematode infections are quite widespread in livestock farms in the Kharkiv region of Ukraine. The extent, intensity of infection, and species composition of helminths varies depending on the animal species. The highest prevalence of infection among farm animals was found in goats – 60%. In chickens, the extent of infection was 44.4%, in pigs and sheep – 34.8% and 33.3%, respectively. The lowest extent of infection was found in calves – 28.6%.

In goats, *Trichostrongylus* spp., *Nematodirus* spp., *Cooperia* spp. were found to be infected and the intensity of infection was 10.0…50.0 helminth eggs per 1 g of faeces; in chickens – *Ascaridia galli, Heterakis gallinarium, Capillaria* spp. with an intensity of infection of 10.0…45.0; in pigs – *Ascaris suum*, *Oesophagostomum* spp, *Strongyloides ransomi* with an infection rate of 15.0…45.0; in sheep and calves – *Haemonchus* sp., *Nematodirus* spp., *Ostertagia* spp., and an infection rate of 25.0 and 25.0…150.0 helminth eggs per 1 g of faeces, respectively. In dogs, the infection rate of *Toxocara canis, Toxascaris leonina, Ancylostoma* spp. and *Uncinaria* spp. was found; the extensive infection rate was 66.7% and the intensity of infection was 15.0…35.0 worm eggs per 1 g of faeces.

It was found that anthelmintic preparations with the active ingredient levamisole showed a pronounced therapeutic effect in the treatment of nematode infections in animals. The use of levamisole preparations according to the proposed regimens on Day 5 of the study reduced the extent of the infection by 50%, and starting from Day 14, no helminth eggs were detected in the faeces of animals. During the study period, no deterioration in clinical condition or side effects were observed in animals treated with preparations No. 1 and No. 2. It was found that poultry meat on Day 3, pig meat on Day 7, and meat of calves and sheep on Day 11 after treatment with levamisole showed no signs of toxicity and could be sent for processing by meat market operators.

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CONFLICT OF INTEREST

The authors of this study declare no conflict of interest.

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Ефективність використання ангельмінтиків на основі левамізолу

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Анотація. Паразитарні захворювання тварин наносять великі збитки галузі тваринництва та потребують постійного моніторингу та боротьби. Метою роботи було провести моніторинг поголів'я тварин (телят, кіз, овець, свиней, собак, курей) на наявність збудників гельмінтозів, визначити терапевтичну ефективність препаратів на основі левамізолу та загальну токсичність м'яса дослідних тварин за використання тест-культури Colpoda steinii. У період 2020-2022 років виявлено значне поширення інвазійних захворювань тварин в Харківській області України. При дослідженні 3500 голів телят у 1000 (28.6 %) було встановлено стійку інвазованість нематодами з інтенсивністю від 25.0 до 150.0 яєць гельмінтів в 1 г фекалій. У кіз інтенсивність інвазії ендопаразитами складала від 10.0 до 15.0 яєць гельмінтів в 1 г фекалій, тоді як у овець цей показник сягав 25.0 яєць гельмінтів в 1 г фекалій. При дослідженні фекалій від свиней у 800 (34.8 %) пробах виявлено наявність яєць гельмінтів, при цьому моноінвазію виявлено в 300 пробах (37.5 %). При дослідженні фекалій від собак було виявлено 10 (66.7 %) позитивних проб. При дослідженні посліду від курей у 200 (44.4 %) позитивних проб встановлено наявність яєць гельмінтів. Застосування препаративних форм левамізолу дозволяє знизити екстенсивність інвазії у тварин на 50 % вже на 5 добу. Із 14 доби по 30 добу спостереження в фекаліях тварин яєць гельмінтів не виявляли, отже екстенсефективність досліджуваних засобів у сучасних умовах складає 100 %. М'ясо, отримане від сільськогосподарських тварин (свиней, телят, овець) оброблених препаратами на основі левомізолу проявляє ознаки загальної токсичності протягом 5-9 діб після застосування препаратів: 5 діб – для свиней та 9 діб – для телят та овець. У той же час, м'ясо отримате від птиці (курчат) обробленої препаратами на основі левомізолу проявляє ознаки загальної токсичності протягом 2 діб після закінчення курсу лікування

Ключові слова: левамізол; ендопаразити; яйця гельмінтів; протипаразитарний засіб; екстенсивність та інтенсивність інвазії; м'ясо; токсичність