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EFFECTIVENESS OF ALBENDAZOLE-BASED ANTI-PARASITIC DRUGS UNDER MODERN CONDITIONS

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Summary. An important problem in veterinary medicine is still the control of parasitic diseases of farm and domestic animals. The market of antiparasitic drugs is widely represented by anthelmintics based on albendozole, both imported and domestic, but data on the effectiveness of these drugs are currently insufficient. The aim of the research was to determine in the comparative aspect the effectiveness of the use of antiparasitic drugs in different forms with the content of albendazole in different species of animals. In the previous stage of the studies the experimental animals were diagnosed with invasions. The most common infections in cattle were dictyocaulosis and fasciolosis; *Trichostrongylus colubriformis, Cooperia oncophora, Oesophagostomum radiatum* were not detected. No causative agent of *Dictyocaulus vivaparus* infection was detected in horses. The most common infection in dogs and cats was toxacariasis, and in mink the most common was infection wih *Uncinaria* spp. Along with this, no *Taenia solium* and *Diphyllobothrium latum* eggs were detected in dogs, and *Opisthorchis felineus, Taenia solium*, *Diphyllobothrium latum* were not detected in cats. After the use of preparative forms of albendazole in sick animals for 2–5 days, the presence of dead sexually mature nematodes and helminth eggs were noted in the feces of animals. The efficacy of albendazole drugs regarding helminthiasis in farm and domestic animals was 100%

Keywords: ruminants, horses, dogs, cats, minks, helminths

Introduction. Parasitic diseases of farm animals cause significant economic loses to the livestock industry and reduce the quality of their products (Taylor, 2012; Fitzpatrick, 2013; Majeed et al., 2015; Paliy et al., 2018).

Prevention and control of parasitic animal diseases is a mandatory step in general economic and veterinary activities in any agricultural enterprise (Thamsborg et al., 2010; Takeuchi-Storm et al., 2019; Paliy et al., 2020a). These measures should be carried out in a scientifically sound approach with an understanding of both the existing epizootic situation and the use of certain preparative forms (Henrioud, 2011; Paliy et al., 2020b).

The most common helminthiases that cause the most significant loses to livestock farming are fasciolosis, dicroceliosis, strongylatosis of the gastrointestinal tract, dictyocaulosis, etc. (Khanjari et al., 2014; Ezatpour et al., 2015). Ruminants are most often affected by various types of helminths, the most common of which are gastrointestinal nematodes, pulmonary helminths and hepatic trematodes.

These helminths can cause serious diseases, adversely affect animal productivity (Almeida et al., 2010; Charlier et al., 2015). Invasive diseases pose a great danger to young animals and poultry, as they are more likely to have mixed infections (Bogach et al., 2021). The treatment of parasitic diseases of farm animals remains an important problem in veterinary medicine (Bahk et al., 2018; Paliy et al., 2020a, 2020b; Dantas-Torres et al., 2020).

Science and practice have accumulated considerable experience in the use of various antiparasitic drugs in animal husbandry (Matos et al., 2015; Bustnes et al., 2006; Paliy et al., 2021b, 2021c). Thus, in 1976 in the United States, 'Smith Kline & French Laboratory' synthesized a drug called albendazole by selective search among benzimidazole derivatives.

Chemical name of albendazole: [5-(Propylthio)-1H-benzimidazol-2-yl] carbamic acid methyl ester is a very fine powder with a particle size of less than 50 μm, matte white, stable for two years when stored at room temperature. Among the many benzimidazole derivatives, albendazole is essentially the only drug that, in addition to nematodes, is effective against cestodes and trematodes (Seifu et al., 2019; Horton, 2000).

Its effect on helminths is quite complex, based on interference in the energy metabolism of parasites and inhibition of fumarate reductase — an enzyme of the Krebs cycle, which leads to lower glycogen levels and death of parasites from depletion, because the process is 30 times more intense in parasite cells than in their host cells. In some helminth species, albendazole inhibits protein synthesis (John and Petri, 2006).

Albendazole is used in veterinary medicine to treat helminthiasis in cattle, sheep, goats, horses, pigs, dogs, cats, fur animals and poultry (Demeler et al., 2009). For veterinary use, albendazole is available in powder, tablet, suspension and gel form. The new dosage form 'gel' significantly increases the effectiveness and speed of the drug. In addition, the shape of the gel facilitates the feeding of the drug, especially for cats and dogs, which protects animals from excessive stress and provides confidence that they have received the full dose.

The aim of the research was to determine in the comparative aspect the effectiveness of the use of

antiparasitic drugs in different forms with the content of albendazole in different species of animals.

Materials and methods. In accordance with the objectives of the study visual and microscopic methods were used in accordance with the practical manual (Vasil'kova, 1955). Intravital diagnostics of helminthiasis, determination of the number of helminth eggs, identification of pathogens by microscopic method were conducted (Halat et al., 2009). The mean intensity (MI) was determined by counting the number of helminth eggs in the field of view of the microscope.

The following animals were selected for the experiment: cows (n = 30), goats (n = 30), sheep (n = 30), horses (n = 10), dogs (n = 18), cats (n = 20), minks (n = 15) of different breeds and ages. During the clinical examination, the main attention was paid to fatness, general state and keeping of animals. To establish a preliminary diagnosis, fecal samples were taken from the animals for laboratory testing.

Two groups were formed of the animals diagnosed with helminthiasis: the first group of animals was given the drug No. 1 (1 ml of the drug contains the active substance albendazole — 100 mg; excipients: propylene glycol, xanthan gum. Drug form — gel for oral use, once individually with food, without diet). Animals of the second experimental group were given drug No. 2 (1 ml of the drug contains the active substance albendazole — 100 mg; excipients — up to 1 ml. Drug form — suspension).

The dosage of drugs for the treatment of animals was:

— cattle: for nematodes and cestodes — 0.75 ml per 10 kg of animal weight once, for trematodes — 1.0 ml per 10 kg of weight twice;

— small cattle: for nematodes and cestodes — 0.5 ml per 10 kg of animal weight once, for trematodes — 1.0 ml per 10 kg of weight twice;

— horses: for nematodes and cestodes — 0.5 ml per 10 kg of animal weight, once;

— dogs, cats, minks: for nematodes and cestodes — 2.5 ml per 10 kg of animal weight, once.

Clinical examination of animals was performed during and after treatment. 5, 10, 15, and 30 days after treatment, the results of studies were recorded based on the clinical examination of treated animals, detection of helminth eggs in fecal samples. Prevalence of infection after treatment and effectiveness of drugs were determined. The animals of the first and second groups were cared identically.

Examination of fecal samples for the presence of helminth eggs was performed by the Fülleborn flotation method and the Baermann method (Kotel'nikov, 1984) using a light microscope at magnification × 100. For identification, the detected helminth eggs were examined at magnification × 400.

Prevalence (P) of infection was determined by the formula:

$$P = \frac{X}{Y} \times 100,$$

where: P — prevalence of infection, %;
X — number of fecal samples in which helminth eggs were detected;
Y — total number of fecal samples;
100 — conversion factor into percent.

Effectiveness (E) of the drugs was calculated by the number of treated animals in percent that were completely free of parasites.

Experiments on animals were conducted following the recommendations of the 'European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes' (CE, 1986) and Council Directive 86/609/EEC (CEC, 1986), and in accordance with Art. 26 of the Law of Ukraine No. 3447-IV of 21.02.2006 'About protection of animals from cruel treatment' (VRU, 2006) and basic bioethical principles (Simmonds, 2017).

The research program was reviewed and approved by the Bioethics Commission of the National Scientific Center 'Institute of Experimental and Clinical Veterinary Medicine' in the current order.

Results and discussions. During the clinical examination of farm animals (cattle, small cattle, horses), we observed in some of them weight loss, indigestion, dullness of the coat. It was found that with a balanced diet, adult animals and young animals did not gain weight. Fecal samples were taken from all animals for laboratory testing (Table 1).

Table 1 — Prevalence (P) and mean intensity (MI) of helminthic infection in cattle (n = 30), sheep (n = 30), goats (n = 30), and horses (n = 10)

Animal species	Species of helminths	P, %	MI, the number of eggs, larvae of helminths in the microscope, pcs.
Cattle	*Ostertagia* spp.	11.4	3.5 ± 1.5
	Trichostrongylus colubriformis	0.0	—
	Cooperia oncophora	0.0	—
	Oesophagostomum radiatum	0.0	—
	Nematodirus spathiger	10.0	1.5 ± 0.5
	Dictyocaulus vivaparus	28.6	15.0 ± 3.0
	Fasciola hepatica	23.3	2.0 ± 1.0
Sheep	*Haemonchus contortus*	11.4	1.5 ± 0.5
	Nematodirus spathiger	13.3	1.0 ± 0.5
	Dictyocaulus filaria	30.0	11.5 ± 3.5
	Moniezia expansa	21.7	10.5 ± 3.5
Goats	*Haemonchus contortus*	20.0	1.5 ± 0.5
	Nematodirus spathiger	13.3	1.0 ± 0.5
	Dictyocaulus filaria	50.0	10.5 ± 3.5
	Moniezia expansa	6.6	8.5 ± 2.5
Horses	*Anoplochephala magna*	6.6	5.5 ± 0.5
	Dictyocaulus vivaparus	0.0	—

According to the results of research (Table 1) it was found that dictyocaulosis with prevalence 28.6% and fasciolosis with prevalence of 23.3% were the most common infections in cattle. In goats and sheep, the prevalence for dictyocaulosis was 50% and 30%, respectively.

Along with this, we did not detect pathogens *Trichostrongylus colubriformis*, *Cooperia oncophora*, *Oesophagostomum radiatum* in cattle. No causative agent of *Dictyocaulus vivaparus* infection was detected in horses.

Examination of domestic animals (dogs, cats, minks) revealed animals with signs of indigestion, changes in their physiological state. To diagnose diseases in animals, samples were taken and studied (Table 2).

Table 2 — Prevalence (P) and mean intensity (MI) of helminthic infection in dogs (n = 18), cats (n = 20), and minks (n = 15)

Animal species	Species of helminths	P, %	MI, the number of eggs, larvae of helminths in the microscope, pcs.
Dogs	*Toxocara canis*	38.8	1.8 ± 0.2
	Toxascaris leonina	33.3	13.6 ± 1.4
	Dipylidium caninum	27.7	1.5 ± 0.5
	Uncinaria spp.	11.1	1.0 ± 0.5
	Ancylostoma spp.	5.5	1.0 ± 0.5
	Trichocephalus spp.	4.4	0.5 ± 0.5
	Taenia solium	0.0	—
	Diphyllobothrium latum	0.0	—
Cats	*Opisthorchis felineus*	0.0	—
	Toxascaris leonina	35.0	13.6 ± 1.4
	Dipylidium caninum	20.0	12.5 ± 0.5
	Uncinaria spp.	10.0	1.0 ± 0.5
	Taenia solium	0.0	—
	Diphyllobothrium latum	0.0	—
Minks	*Uncinaria* spp.	20.5	1.0 ± 0.5
	Ancylostoma spp.	6.6	0.5 ± 0.5
	Toxocara canis	13.3	1.0 ± 0.5
	Dipylidium caninum	6.6	0.5 ± 0.5

According to the results of the studies presented in Table 2, toxocariasis was the most common in dogs and cats, and the prevalence was 38.8% and 35.0%, respectively. In mink, the *Uncinaria* spp. infection was the most common, and the prevalence was 20.5%. Eggs of *Taenia solium* and *Diphyllobothrium latum* were not found in dogs. *Opisthorchis felineus*, *Taenia solium*, and *Diphyllobothrium latum* were not found in cats.

In order to treat animals diagnosed with parasitic diseases, they were given anthelmintics with the active substance albendazole. The results of the study of the effectiveness of experimental drugs in helminthic invasions of cattle, small cattle, and horses for their treatment are presented in Table 3.

Table 3 — Effectiveness of anthelmintic drugs in cases of helminthic infection of farm animals

Animal group	Before treatment		After treatment							
			5th day		10th day		15th day		30th day	
	P, %	Average MI, psc.	P, %	Average MI, psc.	P, %	Average MI, psc.	P, %	Average MI, psc.	P, %	Average MI, psc.
Cattle										
Group I (n = 7)	100.0	6.25	15.0	1.5	0.0	0.0	0.0	0.0	0.0	0.0
Group II (n = 5)	100.0	6.50	15.0	1.0	0.0	0.0	0.0	0.0	0.0	0.0
Sheep										
Group I (n = 5)	100.0	29.40	20.0	1.6	0.0	0.0	0.0	0.0	0.0	0.0
Group II (n = 5)	100.0	26.80	20.0	1.2	0.0	0.0	0.0	0.0	0.0	0.0
Goats										
Group I (n = 4)	100.0	27.50	25.0	2.1	0.0	0.0	0.0	0.0	0.0	0.0
Group II (n = 4)	100.0	28.00	25.0	2.5	0.0	0.0	0.0	0.0	0.0	0.0
Horses										
Group I (n = 5)	100.0	6.50	20.0	0.5	0.0	0.0	0.0	0.0	0.0	0.0
Group II (n = 5)	100.0	6.00	20.0	1.0	0.0	0.0	0.0	0.0	0.0	0.0

After the use of experimental drugs in farm animals (cattle, small cattle, and horses) from the 2nd to the 5th day in the feces of animals the presence of dead adult nematodes was noted. In some animals in the feces we found a small number of eggs of other helminths up to 5th day. In animals, there was an improvement in appetite, normalization of the digestive process. In some animals, especially goats, thirst was observed on the first day after application of the drugs. From the 10th day after the use of anthelmintics, in the samples of feces from animals adult helminths and their eggs were not detected.

The results of the study of the effectiveness of experimental drugs in helminthic infections of dogs, cats, and minks before and after their treatment are presented in Table 4.

After the application of experimental drugs in dogs, cats, and minks, 100% effectiveness was observed after 5th day. Therefore, albendazole-based drugs are highly effective against nematodes, cestodes and trematodes of animals.

The etiological factors of parasitic animal diseases are a number of both endo- and ectoparasites (Atehmengo and Nnagbo, 2014; Paliy et al., 2021a).

Table 4 — Effectiveness of anthelmintic drugs in cases of helminthic infection of domestic animals

Animal group	Before treatment		After treatment							
			5th day		10th day		15th day		30th day	
	P, %	Average MI, psc.	P, %	Average MI, psc.	P, %	Average MI, psc.	P, %	Average MI, psc.	P, %	Average MI, psc.
Dogs										
Group I (n = 5)	100.0	16.80	20.0	7.5	0.0	0.0	0.0	0.0	0.0	0.0
Group II (n = 5)	100.0	16.75	20.0	7.0	0.0	0.0	0.0	0.0	0.0	0.0
Cats										
Group I (n = 5)	100.0	15.80	20.0	6.5	0.0	0.0	0.0	0.0	0.0	0.0
Group II (n = 5)	100.0	15.50	20.0	6.0	0.0	0.0	0.0	0.0	0.0	0.0
Minks										
Group I (n = 3)	100.0	5.50	33.3	0.5	0.0	0.0	0.0	0.0	0.0	0.0
Group II (n = 3)	100.0	5.00	33.3	0.5	0.0	0.0	0.0	0.0	0.0	0.0

Changes in the conditions of their existence in the environment directly affect the manifestation of the invasion of the final host (Bogach et al., 2020). The spread of parasitic diseases is facilitated by the uncontrolled reproduction of stray animals, as well as the contamination of pasture with helminth eggs by sick animals (Paliy et al., 2019; Verheyden et al., 2020).

During diagnostic tests we found a number of helminths in farm and domestic animals. Cases of bovine diseases caused by *Trichostrongylus colubriformis* have been reported in many countries, including Iran, Japan, Thailand, South Korea, China, the United States, and Australia (Ghadirian, 1977; Shahbazi et al., 2012).

In Ukraine, cases are registered sporadically. *Cooperia oncophora* is a gastrointestinal nematode of the genus *Cooperia*, which belongs to the group of trichostrongylides parasitizing in ruminants (Amarante et al., 2014). Nematodes of the genus *Cooperia* parasitize in the small intestine of domestic and wild ruminants. In fact, *Cooperia* spp. considered less pathogenic than other species of bovine and ovine nematodes. A large number of these helminths can significantly reduce the productivity of host animals, as the invasion is associated with lack of appetite and insufficient growth of animals (Ramünke et al., 2018).

Generally, higher temperatures and humid environments are more favorable for these parasites (Gibbons, 1981). The parasite *Oesophagostomum radiatum* is a nematode that causes esophagostomosis. According to studies by other scientists, sheep are most often affected by this parasite in mountainous areas, sometimes even 100% (Magomedov et al., 2014).

The parasite *Taenia solium*, porcine tapeworm, is not detected in the feces of dogs and cats, as the dog is only an intermediate host (García et al., 2003).

The causative agent of diphyllobothrium is *Diphyllobothrium latum*, an intestinal parasitic zoonotic invasion. The most common cause of diphyllobothriosis in humans is the consumption of fish that contain invasive larvae of the genus *Diphyllobothrium*, which cause invasive disease (Ito and Budke, 2014; Le Bailly and Bouchet, 2013). *Diphyllobothrium latum* eggs were not found in the feces of dogs and cats, as they are not the definitive hosts of this helminth.

Opisthorchiasis is caused by *Opisthorchis felineus*. The main source of invasion is humans. Of the various carnivorous species (definitive hosts), the fur animal otter plays an important role in the spread of opisthorchiasis, which has close contact with the intermediate (freshwater mollusk *Bithinia leachi*) and additional hosts (carp) (Pakharukova and Mordvinov, 2016).

According to other researchers (Glamazdin et al., 2013), albendazole and its dosage forms are widely used to control animal helminthiasis. Our results are consistent with the results of other researchers regarding the high anthelmintic effect of drugs with the active substance albendazole.

Conclusions. Veterinary drugs based on albendazole in the form of gel and suspension are effective in the treatment of farm and domestic animals with helminthic infections, they are well tolerated and do not give side effects in the clinical state of animals.

Albendazole-based antiparasitic drugs (gel/suspension) are effective in the treatment of cattle, sheep, goats, horses, dogs, cats, and minks with nematode, cestode and trematode infections.

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