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ORIGINAL ARTICLE

Effectiveness of a modern antiparasitic agent for deworming in domestic animals

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Parasitic diseases continue to account for a significant proportion of overall morbidity in many parts of the world despite improved living conditions and increased awareness of health issues. The creation of innovative veterinary antiparasitic agents is a promising area of modern veterinary pharmacy. The pathogens *Dipylidium caninum*, *Ancylostoma caninum*, *Toxocara canis*, *Toxocaris leonina* were identified in the study of stray dogs (n=12). Eggs of *Dipylidium caninum*, *Toxocara mystax*, and *Toxocaris leonina* were found during cats' examination (n=15). Both mono and mixed invasions have been diagnosed in animals. We established that the floor and inventory were contaminated with exogenous forms of helminths at an extent of 100% after keeping animals in the shelter's enclosures. An innovative antiparasitic agent was used to treat animals. One tablet (0.5 g) contains the following active ingredients such as pyrantel pamoate (150±0.5 mg), praziquantel (50±0.5 mg), and auxiliary substances (lactose, microcrystalline cellulose, calcium stearate, sodium chloride, food flavoring "meat", povidone K-30 and potato starch). We estimated high antiparasitic agents' extensive efficiency (100%) at mono and mixed invasions in dogs and cats.
Keywords: dogs, cats, helminth eggs, antiparasitic agent, extensiveness and intensity of invasion.

Introduction

In recent years, many countries have experienced dramatic changes in climate and landscape due to urbanization processes, which contributes to a significant change in biodiversity in these regions (Bogach et al., 2020). Since over 75% of human diseases are of zoonotic origin, it is crucial to understand the dynamics of interactions between nature, pets, and humans and conduct more targeted studies of the transmission of zoonotic parasites (Mackenstedt et al., 2015). The emergence of new diseases can be caused by many factors, including climate change, global warming, population mobility, animal movements, globalization of trade, social and cultural factors, innovative agricultural practices, inappropriate or overuse of certain drugs that lead to resistance of pathogens (Yan et al., 2010; Atehmengo & Nnagbo, 2014).

Infectious agents can be transmitted by the fecal-oral route, by direct contact through bites or scratches, indirectly different transmissive vectors, and accidentally due to environmental contamination with pathogenic microorganisms, including aerosol of dried animal feces (Fong, 2017). Mammals can be infected with a wide range of gastrointestinal parasites, containing exogenous forms presented in feces and subsequently contaminate soil and water (Nunn et al., 2011). It has also been found that double-winged insects contribute to the spread of helminth eggs in natural foci. There were animal ectoparasites among them (Ibrahim et al., 2018).

The increase in the number of stray animals on the streets causes environmental pollution by exogenous forms of helminths, the spread of invasive diseases among domestic animals, in particular helminthiases (Paliy et al., 2019). Free-roaming cat populations pose a significant threat to public health and are the source of many zoonotic diseases, including rabies, toxoplasmosis, plague, and tularemia. Some of these diseases cause serious health problems in humans and even death

(Gerhold & Jessup 2013). Foodborne parasitic zoonoses cause severe illness and even death in humans and animals worldwide and have both epidemiological and socioeconomic implications (Zhou et al., 2008; Day, 2011). One of the severe parasitic diseases is hookworm disease, which is widespread throughout the world. An infection has been found in approximately one billion people (Wang et al., 2010).
A *Toxocara canis* in dogs and *Toxocara cati* in cats can cause significant pathology in humans. Seroprevalence of antibodies to toxocariasis in humans varies depending on geographic location, socioeconomic status, and dietary habits. Geophagy and low educational level are risk factors for infection (Lee et al., 2010). The problem of dipylidiosis in domestic animals deserves special attention (Shin & Liao, 2002; Saini et al., 2016). This disease is also dangerous for humans, who can be accidental hosts when ingested cysticercoid larvae (Narasimham et al., 2013; García-Agudo et al., 2014).
Helminths *Taenia* spp. can cause cysticercosis and coenurosis in a wide range of intermediate hosts, including humans. Most dog teniids are widespread throughout the world, but there is little information on the species composition and frequency of indication of this pathogen (Mulinge et al., 2020). A *Hydatigera taeniaeformis* is one of the widespread tapeworms throughout the world (Guo, 2020). Thus, timely diagnosis, treatment, and prevention of helminthiasis among stray and domestic animals have great sanitary and epizootic significance, especially in cities. Successful prevention of helminthiases in domestic animals (dogs and cats) is possible when highly effective veterinary drugs are available. Expensive imported veterinary drugs represent the Ukrainian market. Often, recommendations for the use of drugs are developed without considering the existing epizootic situation, acquired resistance of pathogens, and local factors' environmental impact. Along with this, the domestic import-substituting drugs' arsenal is somewhat limited (Paliy et al., 2020d).
Well-being for these diseases provides animal owners with the necessary range of practical and inexpensive means of combating helminthiases in convenient forms, which can be achieved only through the development and production of highly effective competitive domestic medicines or through the improvement of already known veterinary drugs (Woods et al., 2011; Monzote, 2014; Paliy et al., 2020d). The therapeutic effectiveness of anthelmintics depends primarily on the active substance's chemical activity (Skinner-Adams et al., 2016). However, it was found that the dosage form and manufacturing technology of drugs are also essential and their physical state, the properties of the constituent components, and the route of administration into the body (Pink et al., 2005; Mukherjee et al., 2016). The study of their toxic effects on biological objects is an intermediate stage in testing new chemical compounds (Bondarchuk et al., 2019; Orobchenko et al., 2020; Kovalenko et al., 2020).
The research aim was to estimate the suggested innovative complex veterinary drugs.

Materials and methods

An innovative antiparasitic agent was used for research. One tablet (0.5 g) contains active ingredients such as pyrantel pamoate (150±0.5 mg), praziquantel (50±0.5 mg), and auxiliary substances (lactose, microcrystalline cellulose, calcium stearate, sodium chloride, food flavoring "meat", povidone K-30 and potato starch). Pyrantel pamoate is effective against nematodes (round helminths). It affects their cholinergic receptors, which leads to irreversible spastic paralysis of the parasites (St Georgiev, 2001). Pyrantel pamoate is almost not absorbed by the intestines, and its anthelmintic effect is prolonged due to this property. Nematodes are excreted from animals' bodies, predominantly unchanged with feces (Mackenstedt et al., 1993; Arion et al., 2018).
Praziquantel is active against cestodes (tapeworms). It increases the permeability of membranes for calcium ions, causes an increase in muscle activity, is accompanied by muscle contraction and spastic paralysis, and destroys the outer cover of adult forms of parasites (Tchuem Tchuenté et al., 2013; Ghazy et al., 2020). The experiments were conducted in the Laboratory of Veterinary Sanitation and Parasitology of the National Scientific Center "Institute of Experimental and Clinical Veterinary Medicine" (Kharkiv, Ukraine) and based on an animal shelter (Balakleya, Kharkiv region, Ukraine). Dogs (n=12) and cats (n=15) of various breeds and ages were used as experimental animals.
Research scheme:
1) Clinical examination of animals in the shelter, making a preliminary diagnosis, taking fecal samples for laboratory research, constant clinical observation of the physiological state of experimental animals;
2) Microscopic examination of samples with the determination of pathogens of helminthic diseases in the biological material, their identification, the establishment of the extensiveness of invasion in dogs and cats;
3) Administration of the drug (individually), keeping the animals in the shelter, taking fecal samples for laboratory research 5, 10, and 15 days, and one month after the drug's last use. Determination of the extensive efficiency of use of the drug;
4) Daily clinical examination of the state of health of the experimental animals during the experiment's entire period.
Laboratory glassware, microscope, refrigerator, Petri dishes, slides and coverslips, reagents for microscopic studies (saturated NaCl solution, glycerin), fecal samples from experimental animals (dogs, cats) were used in the research.
Visual and microscopic methods carried out the studies per the assigned tasks (Taglioretti et al., 2014). Vital diagnostics of helminthiasis were conducted, and the number of helminth eggs was determined. The pathogens were identified by a microscopic method. The intensity of invasion was determined by counting the number of helminth eggs in 1 g of feces.
The animals of the experimental groups were provided with appropriate conditions of keeping. Clinical examination of the animals was carried out before, during, and after treatment. The drug was administered to the animals once *per os* with a small amount of feed individually (Table 1).
Accounting of research results was conducted based on examinations of treated animals and detection of helminth eggs in fecal samples in 5, 10, 15, and 30 days after treatment. The extensiveness of invasion after treatment and the extensibility of the drug were also determined.
The Study of feces was carried out according to the Fueleborn flotation method according to GOST 26283 (ST SEV 2647-80) using a light microscope with a magnification (× 100). The found helminth eggs were examined at magnification (× 400) with

their subsequent identification. The assessment of the drug's antiparasitic action was carried out when the clinical signs of the disease disappeared, and there were no exogenous forms of parasites in animal feces (Seyoum et al., 2017).

Table 1. Dosage of the antiparasitic agent

Animals	Animal body weight, kg	Dosage, tablets
Dogs, puppies	up to 2	1/4
Dogs	2-5	1/2
	6-10	1
	11-20	2
	21-30	3
	31-40	4
	41-50	5
Kittens	–	1/4
Cats	–	1/2

We carried out the investigations of washings from the enclosures where the experimental animals were kept by the flotation method. Samples from feeders, walls, and floors were taken to determine the sanitary level of environmental pollution by exogenous forms of helminths in animal enclosures. Samples of washings were taken with cotton-gauze swabs soaked in sterile saline. The formula determined the extent of invasion:

$$\mathrm{EI} = \frac{x}{y} \times 100$$

where: EI – extensiveness of invasion;
x – number of fecal samples where helminth eggs were detected;
y – total number of fecal samples;
100 – conversion factor to percent.
The drug's extensive efficiency (EE) was calculated by the number of treated animals that were completely free from invasion in a percentage. Experiments with animals were performed according to current bioethical requirements (Festing & Wilkinson, 2007; Kabene & Baadel, 2019).

Results and discussion

We established that weight loss, indigestion, and dullness of fur were found in some dogs and cats due to clinical examination. Animals do not gain weight; young animals do not grow well with an adequate feeding diet. We collected fecal samples from all animals for laboratory study (Table 2) and sampled the swabs for research contamination by exogenous helminths from the room where the animals were kept (Table 3).

Table 2. Determination of the extensiveness and intensity of infestation by helminths (qualitative and quantitative composition) in dogs (n=12) and cats (n=15)

Animals	Helminth species	The extensiveness of invasion, %	The intensity of invasion, the number of helminth eggs in 1 g of feces
Dogs	*Dipylidium caninum*	100	13.1±1.0
	Ancylostoma caninum	20	7.5±4.0
	Toxocara canis	50	3.5±1.5
	Toxocaris leonina	10	3.5±2.5
Cats	*Dipylidium caninum*	66.7	11.5±2.5
	Toxocara mystax	100	3.5±1.5
	Toxocaris leonina	20	2.5±1.5

We registered monoinvasion in three dogs, which accounted for 25% of the surveyed animals. We also determined the invasion caused by three helminth species (*Dipylidium caninum*, *Toxocaris leonina*, and *Ancylostoma caninum*) in one dog. Monoinvasion was found in two cats only that accounted for 13.3% of the number of examined animals.
Studies have shown that the premises' dishes and walls where the experimental animals were kept did not contain the helminth eggs. Helminth eggs were not isolated. Simultaneously, the floor and equipment in dog enclosures and cat care before the anthelmintic use were contaminated with eggs of various helminths in 100% of cases. The number of helminth eggs varied from 2.5 to 5.5 in 1 sample. We found that exogenous forms of helminths are contaminated with the floor and trays in the premises for cats with an invasion rate of 20 and 60%, respectively. The average intensity of invasion was 1.5 helminth eggs. After the formation of research groups of animals, an antiparasitic drug was applied (Table 4).
Table 3. Determination of the extensiveness and intensity of pollution by exogenous forms of helminths in premises for keeping animal

Animals	Objects	The extensiveness of invasion, %	The intensity of invasion, the number of helminth eggs in 1 sample
Dogs	Dishes	–	–
	Walls	–	–
	Flor	100	2.5±1.5
	Inventory	100	5.5±2.5
Cats	Dishes	–	–
	Walls	–	–
	Flor	20	1.5±0.5
	Trays	60	1.5±0.5
	Inventory	100	4.5±0.5

Note: "–" pollution by exogenous forms of helminths is absent.

Table 4. Therapeutic efficacy of the antiparasitic drug

Animals	Before treatment		After treatment							
	EI, %	II, average	5 days		10 days		15 days		30 days	
			EI, %	II	EI, %	II	EI, %	II	EI, %	II
Dogs (n=12)	100	7.2	16.7	12.5	0	0	0	0	0	0
Cats (n=15)	100	6.8	13.3	7.5	0	0	0	0	0	0

After the drug was administered, we observed 10% of the animals with drowsiness and lack of appetite. The animals did not go near the food but drank much water during the experiment's first day. We registered discharge of sexually mature forms of helminth between the second and sixth day with animal feces. However, we did not observe further complications or changes in the clinical condition of the experimental animals. The extent of invasion in dogs decreased by 83.3% after administering anthelmintic drugs, the average intensity of invasion increased by 73.6% to the average intensity of invasion before treatment; the extent of the invasion in cats decreased by 86.7% after the drug administration on the fifth day; the average intensity of invasion increased by 10.0% to the average intensity of invasion before treatment.

An increase in the intensity of invasion after application of the drug was due to a process when sexually mature females of parasites increase the number of secreted eggs caused by uncontrolled contraction of muscles of the uterus under the action of anthelmintic. From 10 days to 30 days of observation in animals' feces, we did not detect helminth eggs, so the tool's extensibility was 100%. We established that the extensive efficiency (EE) of the antiparasitic drug was 100% in the Study on dogs and cats on mono and mixed invasion of helminths while summarizing the results. Simultaneously, we carried out studies of swabs taken from enclosures where experimental animals were kept for the presence of exogenous forms of helminths (Table 5).

Table 5. Extensiveness and intensity of pollution by exogenous forms of helminths in premises for keeping animals

Animals	Objects	Period of observation							
		Before treatment		After treatment					
				5 days		10 days		30 days	
		EI, %	II	EI, %	II	EI, %	II	EI, %	II
Dogs	Flor	100	2.5±1.5	100	4.5±1.5	0	0	0	0
	Inventory	100	5.5±2.5	100	7.5±2.5	0	0	0	0
Cats	Flor	20	1.5±0.5	40	2.5±0.5	0	0	0	0
	Trays	60	1.5±0.5	100	3.5±0.5	0	0	0	0
	Inventory	100	4.5±0.5	100	5.5±0.5	0	0	0	0

As can be seen from the data in Table 5, pollution by exogenous forms of helminths in enclosures where animals were kept grows on the fifth day after deworming due to the active release of parasites from the animal body treated by the drug. Exogenous forms of helminths in buildings were not detected after 10-30 days, which indicates the absence of their excretion by experimental animals. Parasitic diseases of farm and domestic animals are essential for modern veterinary practice (Epe et al., 2004; Paliy et al., 2018c). The ubiquitous distribution of animal helminths has been established in various geographic zones of the world (Trotz-Williams & Trees, 2003; Traversa et al., 2010; Paliy et al., 2020b).

Climate change and rising global temperatures threaten to disrupt the physical, biological, and ecological life-support systems on which human and animal health depends, which is especially true for changes in various diseases' etiological factors and their uncontrolled spread to new ecological niches and territories (Blashki et al., 2007; Koch & Willesen, 2009). This situation increases biological risks for both animals and humans (Patz et al., 2000). The ability of humanity to respond or adapt to new challenges in epidemiology and epizootiology depends on their magnitude and speed of change, as well as the ability to recognize, effectively contain and control biological threats at an early stage and provide appropriate treatment and prevention (Khasnis & Nettleman, 2005). Timely complex diagnostics of diseases play an important role in control and prevention measures against parasitic invasions (Paliy et al., 2018b; Conboy, 2009). Improvements and new serological, molecular, and imaging diagnostic tests and the development of broad-spectrum chemotherapeutic agents have led to significant reductions in morbidity and mortality caused by parasitic zoonoses (Macpherson, 2005).

There is no convincing alternative to chemical control for parasitic invasions (Shkromada et al., 2019b; Zhang et al., 2019; Paliy et al., 2020d). Many anthelmintics are used, which differ in their spectrum of action, composition, and active substances, to treat animals with parasitic diseases (Venco et al., 2008). Along with this, multiple anthelmintic resistance has been established in *A. caninum* field isolates that indicates a new problem in treating this disease (Kopp et al., 2007; Jimenez Castro et al., 2019). Repeated treatment with lower pyrantel pamoate concentrations will be more effective than higher concentrations given only once (Mackenstedt et al., 1993). Anthelmintic drug resistance has become a significant concern in veterinary medicine and threatens agricultural incomes and animal welfare (Fanning et al., 2010). The molecular and biochemical basis of this resistance is insufficiently studied. The lack of reliable biological and molecular tests means that we cannot monitor the emergence and distribution of resistance alleles and clinical resistance of helminths (Wolstenholme et al., 2004; Kaplan, 2004).

Disinfection of veterinary control facilities is becoming increasingly crucial despite the high level of provision of specific agents in the fight against various etiology diseases (Stegniy et al., 2019; Paliy et al., 2020c). However, the use of disinfectants in specific conditions requires their additional approbation and determination of useful modes of exposure (Paliy et al., 2016; 2018a; Shkromada et al., 2019a). A study and practical application of scientific approaches to use animal parasites' natural enemies is a separate scientific area (Paliy et al., 2018d; 2020a).

Domestic animals' owners should be appropriately informed about zoonotic risks, and veterinarians should organize regular screening and treatment of domestic animals. The establishment of national surveillance programs to determine the incidence and the presence of a specific etiological agent in sick animals is an urgent task today (Lee et al., 2010; White et al., 2017). Wildlife plays a vital role in the epidemiology of parasitic diseases. Control measures, in turn, should focus on minimizing the transmission of pathogens to highly susceptible animal species (Munang'andu et al., 2012). In contrast, the birds (canaries, parrots) pose a potential hazard to human health since they could be carriers and vectors of zoonotic diseases such as chlamydia and salmonellosis, highly pathogenic avian influenza type A (H5N1) (Boseret et al., 2013). There is an urgent need to develop a holistic understanding of migration's potential both to increase and reduce the risk of infection of animals (Mckay & Hoye, 2016).

Understanding the broad patterns of host-parasite associations can help predict the emergence of new diseases in humans, domestic animals, and wildlife that will be important in developing effective programs to control emerging infectious diseases and neglected endemic diseases (Farrell et al., 2013). Parasitic diseases continue to represent a significant part of the overall morbidity in many countries globally, despite improved living conditions and increased awareness of health issues (Harizanov et al., 2020).

Conclusions

Active ingredients such as pyrantel pamoate (150±0.5 mg) and praziquantel (50±0.5 mg) as well as auxiliary substances of lactose, microcrystalline cellulose, calcium stearate, sodium chloride, the flavor of food "meat", povidone K-30, and potato starch are part of the antiparasitic drug. The antiparasitic drug is well tolerated in dogs and cats and does not give side effects and changes in animals' clinical state, and is an effective anthelmintic against cestodes or nematodes.

The investigated veterinary drug can be used for therapeutic and prophylactic deworming in nematodes, cestodes, and mixed nematodes-cestodes invasions of dogs and cats. Our results could expand the range of domestic antiparasitic agents for veterinary medicine.

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