

STUDY OF DRUGS' ANTHELMINTIC EFFICACY IN ANIMAL TREMATODOSES

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Annotation:

This article describes the literature sources and their analysis on the effectiveness of anthelmintic drugs used in practice by scientists of our republic, the CIS, and foreign countries for the treatment and prevention of trematodes among agricultural and wild animals.

Ключевые слова: Трематода, трематодоз

Аннотация:

Ушбу мақолада қишлоқ хўжалиги ва ёввойи ҳайвонлар орасида учрайдиган трематодозларни даволаш ва олдини олиш бўйича республикамиз, МДХ, ҳамда хорижий давлатлар олимлари томонидан кейинги йилларда амалиётда қўлланилиб келинаётган антгельминтик препаратларнинг самарадорлиги бўйича адабиёт манбалари ва уларнинг таҳлили баён этилган.

Аннотация:

В данной статье описаны литературные источники и их анализ по эффективности антгельминтных препаратов, применяемых на практике учеными нашей республики, СНГ и зарубежных стран для лечения и профилактики трематодозов сельскохозяйственных и диких животных.

дегельминтизация, фасциола, парамфистом, антгельминт, инвазия, гельминтоз, биогеоценоз, биоэкология, иммуномодулятор, экосистема, паразитоценоз.

Keywords: trematode, trematode, deworming, fasciole, paramphistome, anhelminth, invasion, helminthiasis, biogeocenosis, bioecology, immunomodulator, ecosystem, parasitocenosis.

Introduction

Parasitic diseases are widespread in all regions of the world. Trematodes occupy an important place among parasitic diseases. The causative agents of these diseases develop in a complex way, in which both biotic and abiotic factors of the terrain play a part. Affecting vital organs, especially the liver, scar, intestines, and circulatory system, they can cause the death of animals and thereby cause great economic damage to animal husbandry.

Over the past decades, domestic and foreign authors have developed and tested a significant number of chemicals with antiparasitic properties. Many of them turned out to be ineffective or toxic.

The Purpose of the Study:

Analysis of the effectiveness of anthelmintic drugs used for the treatment and prevention of trematodes, widespread in our republic and around the world, based on individual studies and literature data.

Literature Review

Based on the results of cattle deworming with albendazole and albendazole plus at a dose of 5 mg/kg of body weight, the authors found that low EE of drugs with fascioliasis were noted: 55.9 and 58.8%, respectively [7].

The author claims that the use of afascil, an injectable drug with subcutaneous administration at a dose of 1 ml per 20 kg, provides a high effect against young forms of fascioles in the summer; at a dose of 1 ml per 40 kg, a 100% effect against sexually mature fascioles; afascocide in the form of granules when administered orally at a dose of 10 mg per kg according to DV, provides a 100% effect against both young and mature fascioles [11].

The researcher recommends using an oxyclozanide suspension of 5% at doses of 12.2 and 10 mg/kg each against sexually mature fasciolas and 15.0 mg/kg against sexually mature paramphistomas of cattle and sheep [26].

For the treatment of bovine paramphistomatosis, the author recommends using the drugs "Alben-Super 20%" at a dose of 7.5 g per 100 kg of body weight and "Ricobendazole" at a dose of 2.0 ml per 100 kg of animal body weight. While [29], the author recommends the use of "Ricobendazole" in fascioliasis at a dose of 4.0 ml per 10 kg of body weight with an efficiency of 90–100% [16].

The author considers it optimal to use drugs such as tegalide, polytrem, bithionol, thiogalol, and fasinex against cattle trematodes, and albendazole is ineffective (EE 56%–68%) [2].

The author tested antiparasitic agents: delcide, fascocide, alben-super, and 10% suspension of albendazole in invasive diseases of cattle in the Middle and Lower Volga regions with a positive effect [4].

Scientists have proposed the use of alfenfrem and antitrem in doses of 75 and 50 mg/kg in bovine fascioliasis with a positive effect [20].

The researcher found out that the use of febtalagranulate at a dose of 90 mg/kg and fezol at a dose of 20 mg/kg once for associative invasions of cattle is optimal [23].

In the literature, there is information not only about the effectiveness of drugs but also about their accumulation in the tissues of fasciolas, their mechanism of action, and their toxic properties.

According to the author, the effectiveness of disalar in treating sheep fascioliasis is 92–98.5%. However, the drug suppresses the effector mechanisms of immunity (the immunoregulation index is 0.6–0.8 units). A large number of drugs, including domestic ones, have been proposed to combat fascioliasis in cattle. However, almost all of these drugs are excreted from the bodies of treated animals for a long time, including with milk, which makes their use difficult for lactating animals, and rafoxanide, fasinex, and ivomek-plus are not recommended for this reason for use in dairy cows. In this regard, it is relevant for veterinary practice to develop an effective anthelmintic (trematode) for the treatment of ruminants, including during lactation. The choice of oxyclozanide is explained by the fact that it is rapidly excreted from the body during the day [31].

Comprehensive preventive measures for trematodes in cattle include general, veterinary, sanitary, and special measures. Of the general measures of

paramount importance in improving the immune status, resistance (immunity) to diseases, are full-fledged balanced feeding of animals and exercise, high-quality cleaning of premises and disinfection of them and manure, grazing animals on reclaimed pasture areas, and changing them while taking into account the bioecology of intermediate hosts (mollusks) [22, 34].

The author suggests a scheme of preimaginal deworming based on the use of phasinex during the period of pasture keeping of animals: 2 months after pasture (end of June-bbeginning of July); at the end of August-bbeginning of September; at the end of October-bbeginning of November [32].

The fight against fascioliasis in animals should be carried out not only with the use of the latest anthelmintics but also with the use of molluscocides and environmental principles [13].

The researcher suggested using the complex drug abictin at a dose of 1 ml per 50 kg of body weight together with the immunostimulator ribotan, which increased the immune status of animals [33].

The author proposed a comprehensive method for the treatment of fascioliasis using fenbendazole, the immunostimulator polyoxidonium, and bifidumbacteria, which led to a change in animal indicators for the better by the 30th day of research [25].

Immunomodulators contribute to the realization of the potential of cattle, the restoration of the immunoregulatory index, the increased activity of T-killers, the increased activity of hematopoietic stem cells, and other indicators of immunity.

Immunoparasitan, with an interval of 7 days at a dose of 1.8 ml/hhead, accelerates the maturation of germinal centers and cell migration three times, enhances immunological reactions, and causes stimulation of T- and B-lymphocytes.

Ribotan, given three times with an interval of 10 days and at a dose of 1.5 ml, stimulates the functioning of T-lymphocytes, the production of appropriate mediators, the activity of mononuclear phagocytes, and has the ability to increase the level of antibodies, the effect of vaccination.

Comprehensive study of fascioles and paramphistomatoses in cattle farms in the Russian Federation's Central District, with the development of new effective measures to combat invasion; seasonal and age dynamics of the epizootic process, as well as the number of intermediate hosts of fascioles and paramphistomates in natural biotopes; development of a diagnostic based on

excretory secretory antigens *Fasciola hepatica* and *Paramphistomum cervi* for enzyme immunization

Anthelmintic drugs have a toxic effect on the organs and tissues of helminths, blocking the processes of gametogenesis and egg development in the uterus, and their use is a powerful anthropogenic factor in regulating the natural ecosystem—parasitocenoses [12].

The author states the high therapeutic efficacy of disalar (rafoxanide) in bovine fascioliasis. The drug has a detrimental effect on sexually mature and primagonal forms of fasciolas. The same author found that the drug is also effective in sheep fascioliasis (92%–98.5%). However, the drug suppresses the effector mechanisms of immunity. The immunoregulation index is 0.6–0.8 units [30].

According to the researcher, based on the results of cattle deworming with albendazole and albendazole plus (at a dose of 5 mg/kg), the low extensibility of these drugs in fascioliasis was noted: 55.9 and 58.8%, respectively [9].

The authors of the group found that the antitrem drug at a dose of 0.25 g/kg is effective in treating fascioliasis and paramphistomosis in cattle [8].

According to a number of scientists, the use of exclusively trematocidal drugs does not allow for productivity restoration in dewormed animals for 4-5 months [1].

Therefore, developments aimed at reducing the toxic properties of anthelmintic drugs while maintaining their effectiveness, as well as the creation of dosage forms that do not have a local, irritating property, are important. The production of anthelmintics rapidly released from the body for lactating animals and products with a pronounced ovicidal effect is promising [6].

As a result of experimental studies, the author determined the 100% effectiveness of the immunomodulator immunoparasitan and the anthelmintic drug disalara in treating bovine fascioliasis. The anthelmintic effect persists for 150 days after treatment in animals [27].

According to many authors, they point out the importance of the following preventive measures for fascioliasis: the right choice of pasture and watering places; changing pastures and watering places 2-3 times per season; and the use of effective drugs for primal deworming and treatment [18].

New, more effective means are being sought for the helminthization of animals since most of the proposed drugs do not have 100% effectiveness. In addition, on the basis of modern achievements in veterinary, medical, and biological science, complex methods of treating animals with fascioliasis (using

immunomodulators and probiotics) as well as preventive measures, including ecological and biological ones, are proposed.

When studying the same drugs, different authors obtained different, sometimes contradictory results. It depends on various reasons: doses, techniques and forms of application, the composition of the diet and the condition of animals, the intensity, localization and species composition of helminths. Furthermore, the use of certain drugs in veterinary practice is irrational due to their high cost and complex method of administration.

According to the literature in the middle of the twentieth century, the main anthelmintics used in paramphistomidosis of animals were carbon tetrachloride and hexachloroethane.

The authors of the group used fasconverm at a dose of 5 mg/kg for bovine paramphistomatosis. The efficiency was 93.4%. [10].

According to the data, a large number of drugs with different efficacies have been proposed to combat trematodes, in particular fasciolas and paramphistomas. Among the imported drugs, levacid (bithionol sulfoxide) should be noted. It is also highly effective in paramphistomatosis. However, in Russia, it is used little because of the high cost. [34].

The researcher used 10 drugs in her experiments with fascioliasis, paramphistomatosis and dicroceliosis: polytrem, tegalid, ursovermit, santel, fazinex, faskoverm, tiagolol, ivomek-plus, fenbendazole, albendazole. Of the drugs used, the most effective for paramphistomatoses were: tegalide IE – 92.2-99.8%; thiagolol IE – 94.8-100%; phasinex IE – 88.6-94.8%; faskoverm IE – 86.8-94.2%. [21].

The author obtained the highest effectiveness of fascicide in paramphistomatosis when it was tested at a dose of 15 mg/kg. The effectiveness of the drug at this dose was 97.02% in the "control test" type experiment and 96.8% in the "critical test" type experiment. The author also tested the drug afascil for paramphistomatoses in cattle at a dose of 2.5, 5.0, or 10.0 mg/kg per DV. The efficiencies were 73.3%, 85.9%, and 93.9%, respectively [24].

Along with therapeutic (anthelmintic) agents for paramphistomatosis, there are a number of preventive measures, the effectiveness of which depends on knowledge of the biology of pathogens, the epidemiology of the disease, local natural conditions, and economic opportunities.

It is important to change pastures in the middle of the season (July-August) and, if possible, alternate them every 2 months; exclude watering from non-flowing

reservoirs; and conduct helminthological assessments of pastures monthly during the grazing period [5].

The author established the immunostimulating properties of polysept, aquafem, and aqualipol. Studies have shown that these drugs have a stimulating effect on immunocompetent cells, whose interactions cause the development of an immune response in animals [15].

From the above data, it should be noted that for widespread use in veterinary practice, anthelmintic preparations must have certain properties and meet certain requirements: the highest anthelmintic efficacy against paraphthisomas of all ages combined with the lowest dosage. In addition, anthelmintics should not have pronounced toxicity as well as embryotropic and cumulative properties.

At the same time, the drugs should be convenient for use in veterinary practice (form of release, frequency and method of administration, compliance with a special diet during deworming, and others). Recommended anthelmintics for wide industrial use should have a relatively low cost; in addition, an important factor is the possibility of unhindered purchase of the drug.

The absence of effective drugs on the domestic market has contributed in recent years to the widespread spread of paramphistomoses in cattle and small cattle. Based on the analysis of domestic and foreign literature, it can be concluded that currently paramphistomatosis of ruminants is very little studied. It is necessary to continue studying the features of the life cycle of a paramphist, the influence of natural-climatic, meteorological, and anthropogenic factors on it, and much more [17, 20; 23, 27].

With the development of immunological research in helminthology, new knowledge has been gained about the multicomponent structure of helminths, including not only species-, genus-, and stadium-specific determinants but also common determinants for various taxonomic groups: antibody heterogeneity has been established, affecting the complexity of relationships in parasite-host systems and manifesting itself both in the protection of the host organism and the occurrence of pathological changes as a result of the development of immediate and delayed types of hypersensitivity reactions [17; 24; 28].

Rolenol at a dose of 1 ml and fasciolide at a dose of 0.5 ml per 10 kg of sheep weight have 100 percent effectiveness in treating chronic fascioliasis. However, rolenol in acute fascioliasis has a detrimental effect on young forms of *F. gigantica*, starting from their 40–42 days of age [3].

The authors point out that in the treatment of fascioliasis, it is necessary to take into account the epizootiological features of the region, the seasonality of the course of diseases, age, and the intensity of invasion [19].

The effectiveness of the tested new anthelmintics in paramphistomatosis is as follows:

Facocide 1 tablespoon per 20 kg of w.m., inside through the mouth, showed EE 58.3%, IE 53.2%, and rafenzene 2.5 ml per 10 kg of w.m., through the mouth, showed EE 80% and IE 86%. For the first time tested against bovine paramphistomatosis, the drug Actlek at a dose of 0.075 ml/kg (for every 100 kg of w.m., 7.5 ml) through the mouth with a small volume (300–400 ml) of water showed 100% extension and intensity effectiveness [14].

The authors conducted a study of luxabendazole. It was found that a single use of the drug reduces infection with fasciolas by 74%–95.5%. The dosage form of the drug (5% emulsion), convenient to use, makes it easy to select individual doses [35].

Immunomodulators, without directly affecting helminths, stimulate biologically active components of immunity in the bodies of animals and normalize the physiological functions of the body [36].

The author studied the antiparasitic effects of drugs from the salicylamide group: oxy clozanide, rafloxanide, niclosamide, klazantel, and resorantel. Closantel and rafloxanide have been found to be effective against hemonchosis and fasciolas in cattle [37].

Conclusions

1. The fight against trematodes in agricultural and wild animals should be carried out in a comprehensive manner, taking into account the peculiarities of biology, ecology, seasonality of the year, intermediate and terminal hosts, and the application of scientific and seasonal schemes of helminthization.
2. Analysis of the literature data shows that the mechanism of action of various anthelmintic drugs is insufficiently studied.
3. The scheme of preimaginal deworming of trematodes in agricultural and wild animals has not been sufficiently studied.
4. Considering the toxic, mutagenic, cumulative, and other mechanisms of action of chemicals used to prevent and treat flukes, we recommend the widespread introduction of immunostimulants and immunomodulators into practice.

The List of Used Literature

1. Abdullaev Kh.S., Kuzmichev V.V., Muzhavlev E.F., and Petrov Yu.F. A complex method of treatment of associative diseases of animals caused by parasitization of fasciolas, dicrocelia, bacteria, and fungi // Collection of scientific translations. "Parasitic and associative diseases of animals and their prevention". – Ivanov. – 1997. – p.91.
2. Abdullaev, H.S. The formation of a parasitic system in the body of cattle and measures to combat parasitosis in the Non-Chernozem zone of the Russian Federation: abstract; dis. Doctor of Veterinary Sciences: 03.00.19, 16.00.03 / Abdullaev Khosrov Sattar-ogly. – Ivanovo, 2007. – 50 p.
3. Avezimbetov Sh.D., "Bioecological and epizootological features of trematodes in cattle and sheep in the Republic of Karakalpakstan" Abstract. diss. candidate of veterinary sciences. - Samarkand: SamSHI. 2007. -15 p.
4. Arisov, M.V. Parasitoses of cattle in the Middle and Lower Volga regions and new chemical agents in the fight against them: abstract of the dissertation of a doctor of veterinary sciences: 03.00.19 / Arisov Mikhail Vladimirovich. – Nizhny Novgorod. – 2008. – 41 p.
5. Arutyunok L.D., Petrosyan R.A., Ecological bases of prevention of trematodoses in ruminants. // Veterinary Medicine. 1992. No.12.P.30
6. Arkhipov I.A. Problems and prospects of creating new medicinal forms of anthelmintics and endectocides for animals // Mat-ly doc. Scientific conf. "Theory and practice of combating parasitic diseases", VIGIS – M. – 1999. - pp. 14–16.
7. Arkhipov I.A. Anthelmintic efficacy of tetraxyphol in trematodes and moniesiosis of ruminants / I.A. Arkhipov, T.P. Veselova, and D.N. Shemyakov // Tr. Vseros. in-ta helminthol. — M., 1999. - T.35 - pp. 20–25.
8. Arkhipov, I.A., and Shemyakov, D.N., "Effectiveness of antitremere in fascioliasis and paramphistomosis of cattle," Veterinary Medicine, 2001, No. 2, pp. 27–29.
9. Arkhipov, I.A., and Shemyakov, D.N. "Efficacy of Microcapsulated Albendazole Plus in Strangilatoses of the Gastrointestinal Tract of Sheep and Fasciolosis of Cows" // Mat-ly dokl. nauch.conf. "Theory and Practice of Combating Parasitic Diseases", VIGIS, M. 1999, pp. 18–20.
10. Arkhipov I.A., Koshevarov N.I., Daugalieva E.H., Shemyakov N.D., and Abramov E.V., Effectiveness of faskoverm boluses in parasitic diseases of sheep and cattle," Veterinary Medicine, 1998, No. 10, pp. 22–24.

11. Bogdanova, O.Y. Parasitosis of cattle and measures to combat them: abstract; dis. ;... Candidate of Vet. Sciences: 03.00.19 / Bogdanova Oksana Yuryevna. – N. Novgorod, 2006. – 20 p.
12. Gerebenschchikov V.M., Bibik O.I., and Nacheva L.V. Deworming as an anthropogenic factor and its pathomorphological justification // Tez.dokl. I scientific conference, Novosibirsk, Departments of Parasitol, Russian Academy of Sciences "Parasites and parasitic diseases in Western Siberia", Novosibirsk, 1996, p.36–37.
13. Gorokhov, V.V. Fasciolesis: as a complex ecological problem / V.V. Gorokhov, N.P. Sorokina // Theory and practice of combating parasitic diseases (zoonoses): Materials of the reports of the scientific conference VIGIS, M. 2002, pp. 97–99.
14. Daminov A.S., "Epizootological and immunological features of trematodes in cows in various biogeochemical regions of the republic" Abstract. Diss. Doctor of Veterinary Sciences.- Samarkand: SamSHI. 2016.-45 p.
15. Daugalieva M.Kh., Kurochkina K.G. "Immunoprophylaxis and immunotherapy of helminthiasis in s-X animals"; "The role of the helminthological school in the development of parasitology. Mater. All-Union. Symposium. M. 1997. P. 18.
16. Zhuravleva A.Z. Helminthiasis of cattle in the farms of the Leningrad region: abstract; dis. Candidate of Veterinary Sciences: 03.00.19, Zhuravleva Aigul Zarifovna, St. Petersburg, 2008, 22 p.
17. Koshevarov N.I., The effectiveness of tetraxyphol in bovine paramphistomatosis," Veterinary Medicine, 1997, No. 5, pp. 30-32,
18. Kumysheva Yu.A. fasciolesis of cattle and its effect on the physico-chemical parameters of slaughter products: abstract. dis.... Candidate of Biological Sciences: 03.00.19 / Yulia Aleksandrovna Kumysheva. – M., 2009. – 22 p.
19. Kurbanov Sh.X., "Trematodes of small horned animals in the south of Uzbekistan" abstract. diss. village. vet. nauk.- Samarkand: Samsxi. 2009.-16 s.
20. Kurochkina M.V. The influence of helminths on the immune status of cattle and the prevention of helminthiasis in state-owned farms in the Central district of the Non-Chernozem zone of the Russian Federation. // Abstract of the dissertation of the Candidate of Veterinary Sciences. - Ivanovo.- 2003.P.18.
21. Laifanov, A.V., Cherepanov, A.A.: Ways of improving cattle from parasitic diseases in the Western region of Russia / A.V. Laifanov, A.A. Cherepanov //

Theory and practice of combating parasitic diseases (zoonoses): Materials of reports of the scientific conference VIGIS. – M. – 2002. – S. 195–196.

22. Latypov, D.G. Helminthiasis of cattle in the Republic of Tatarstan (epizootiology, diagnostics, and therapy): autoref. dis., doct. vet.Sciences: 03.02.11/Latypov Dalis Garipovich. — M., 2010. — 41 p.

23. Loshkareva V.V. Maritogony of trematodes in cattle and optimization of the timing of the use of anthelmintics in the conditions of the Middle Urals. // Autoref.diss.candidate of Veterinary Sciences-M.- 2005.P.18.

24. Mayamsina, E.V., Dynamics of intestinal microflora in cattle with fascioliasis and correction with anthelmintics, probiotics, and immunostimulants: abstract of the dissertation," Candidate of Veterinary Sciences: 03.00.19, 16.00.03 / Mayamsina Elena Vladimirovna; Ivanovo, 2004. - p. 19.

25. Morozova A.V. Pharmaco-toxicological properties and efficacy of a new dosage form of oxyclozanide in trematodoses of ruminants: abstract, dissertation Candidate of Veterinary Sciences: 03.00.19 / Morozova Anna Vladimirovna. – M., 2007. – 24 p.

26. Myakin V.A. Complex therapy in bovine fascioliasis in "Theory and practice of combating parasitic diseases". M.-2001, pp. 166–167.

27. Nikitin V.F. Lifetime diagnostics of paramphistomatoses of cattle— Questions of General and Applied Helminthology M.: USSR Academy of Sciences 1978., Fazlaev R.G. Liorkhoz of cattle in the Southern Urals of Bashkiria (epizootiology, pathogenesis issues, prevention, and control measures). //Autoref.diss.Candidate of Veterinary Sciences.- M.- 1987.P. 20.

28. Ogorodnik S.G. Paramphistomatosis of cattle in the farms of the Novgorod region (epizootiology, control measures): autoref.dis.... Candidate of Veterinary Sciences: 03.00.19 / Sergey Grigorievich Ogorodnik. – St. Petersburg, 2007. – 20 p.

29. Pushkarev A.S. Experience of Treatment of Fasciolosis of Cattle // Collection of Scientific Works "Ecological Parasitology". – Ivanovo, 1998 b, p. 32–33

30. Pushkarev, A.S. The effect of disalar on immunobiological reactivity in fascioliasis of cattle and sheep / A.S. Pushkarev // Veterinary Medicine, 1999. - No. 1. - pp. 28–30.

31. Sazanov, A.M., Strategy and tactics of deworming of animals against fascioliasis," in A.M. Sazanov, "Theory and practice of combating parasitic

diseases: Materials of reports of the scientific conference VIGIS," 2001, pp. 233–235.

32. Saushkin, V.V. Nonspecific immunoprophylaxis and complex therapy for helminthiasis of animals: dis....Doctor of Veterinary Sciences: 03.00.19 / Vasily Vasilyevich Saushkin. – Ivanovo, 2002 – 301 p.

33. Saffiullina R.T., The effectiveness of levacid in fascioliasis of cows and sheep. // Materials of the scientific conference "Topical issues of theoretical and applied trematodology and cestodology". VIGIS, S.-M.- 1997. pp. 140–141.

34. Cherepanov, A.A. Strategy and tactics of antiparasitic measures on livestock farms and complexes in new economic conditions / A.A. Cherepanov // Theory and practice of combating parasitic diseases: Materials of reports of the scientific conference VIGIS. – M. – 2001. – pp. 287–289

35. Ising S. Malotki A.V. Zur wirkung von Luxabendazol gegen Helminthen beim Schaf // pract. Tierarzt. -1990.-№8. S. 52-54.

36. Elson C., Immunocyto-adherence of Rh (D) positive erythrocytes to mononucleated cells from the blood of rhesus isoimmunised individuals / C. Elson, J. Bredley // Arch. Allergy and Ahle. Immunol. – 1977. –V. 40. - № 2.- P. 382-397.

37. Swan G.E. Global, Continental, Country health concerns on the use of veterinary products in animals: Post Graduarte symposium. / G.E.Swan // Department of Community Health, University of Pretoria, 25 March 1999.