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Review

Control of Helminth Infections in Captive Herbivores: An Overview of Experience

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Abstract: There are numerous challenges associated with helminth control in captive animals. The aim of the present paper is to provide an overview of the research on deworming of captive herbivorous mammals, the associated problems and the solutions sought, in order to derive recommendations for practice in the relevant institutions. The research was conducted by searching electronic internet databases and following the bibliographies in the published articles. The articles found are presented in summarized form. Most of the results relate to herbivores of the family Bovidae, followed by the families Cervidae, Equidae, Elephantidae, Camelidae and Giraffidae. Systematic data are presented on the types of anthelmintics used, dosages and application regimens for different animal species. Anthelmintics were administered at doses similar to or even higher than those used in farm animals, with no evidence of side effects. Treatment results often depended on the animal and parasite species. Incomplete cure, reinfection, and resistance to anthelmintics were the most common problems in the field. Based on the literature reviewed, the optimal prevention measures include the following: quarantine of newly arrived animals; daily or as intensive as possible cleaning of droppings; regular change of substrate in the enclosures; and monitoring of possible infections and their qualitative and quantitative composition (monthly or at least every two months). For treatments and monitoring effectiveness, recommendations include the following: individual assessment of the need for treatment; selective choice of anthelmintics; post-treatment examination between the 10th and 14th day after deworming; carrying out a group treatment after a preliminary drug effect test; conducting mass deworming only in case of a significant increase in fecal egg counts, highly pathogenic helminth species and a deterioration in the condition of the animals. In the future, more attention should be paid to new approaches such as biological control by saprophytic fungi or natural compounds as an alternative to anthelmintics. This would help minimize the use of anthelmintics, protect refugia and allow animals to remain healthy by maintaining a balance with the low levels of parasites present.

Keywords: anthelminthic treatment; captive herbivores; deworming; zoo parasite prevention

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1. Introduction

Terrestrial herbivorous mammals, a group of about 4000 species, live in every major ecosystem on Earth except Antarctica [1]. Despite their cosmopolitan distribution, many species are threatened with extinction. According to the International Union for the Conservation of Nature, 60% of the largest terrestrial herbivores are threatened with extinction and 58% have declining populations [1]. The protection of endangered species is one of the most important challenges facing humanity today and captive breeding (in zoos, rescue centers, reserves, etc.) is an increasingly common alternative to combat this challenge. However, captive breeding also has its pitfalls, and parasitism is one of them.

The negative effects of this biological phenomenon in captive animals are manifold. Massive infection with certain parasite species can be responsible for high morbidity and mortality [2,3]. In addition, parasites can act as a predisposing factor for development of secondary deficiency and infectious diseases. In many cases, the impaired health status of the animals has a negative impact on their reproduction, which is of great importance in the implementation of specialized captive breeding programs for endangered species [4]. Captive animals without adequately controlled parasitism could transmit resistant nematodes to wild populations in the event of reintroduction [5].

The ultimate goal of any parasite control program is to restrict the parasite population to a level below that which has a significant impact on welfare and/or the economy [6]. There are different approaches to parasite control, ranging from therapeutic control, where action is taken only when clinical disease is detected, to strategic control, where steps are taken to anticipate and mitigate the risk of disease and production losses. The main tools for strategic control in herbivores are pasture management, nutrition, vaccination and medication [7]. Recently, increasing attention has been paid to strategies for maintaining refugia that allow animals to be in balance with the parasites they carry while remaining healthy [8].

An overview of parasite diversity in various European zoos revealed that helminths are the most common parasites in herbivores [4]. Medical control of helminths is carried out by administering drugs targeted against parasite stages in the hosts [9]. The most important groups of anthelmintics are benzimidazoles and probenzimidazoles, imidazothiazoles, tetrahydropyrimidines, avermectins, salicylanilides and substituted phenols, piperazines, and organophosphates [10], with benzimidazoles and macrocyclic lactones being the most commonly used in recent times. Benzimidazoles have low toxicity and in some cases can be used at ten times the recommended dose [10]. The greater efficacy and broader spectrum of activity of the second generation benzimidazoles appears to be due to the relative insolubility of these chemicals, which affects the absorption, transport and excretion of the anthelmintic by the host. The macrocyclic lactones have excellent activity at very low doses. Unlike the benzimidazoles, they are very lipophilic and are stored in adipose tissue and the liver after administration, from where they are slowly released, metabolized and excreted, prolonging their action [10].

The selection and application of dewormers is a challenge for veterinarians in the wild for a number of reasons. In most cases, the drugs on the market are intended for livestock and need to be adapted to wildlife species, which comes with the risk of underdosing or poisoning. Problems with handling the animals can mean that parenteral administration is not possible, so most treatments have to be administered orally. Oral administration does not ensure adequate ingestion of the antiparasitics, so some animals will ingest a higher than recommended dose, while others will ingest practically none. Furthermore, continued use of the same drugs would lead to the development of antiparasitic resistance [9,11]. These factors force wildlife veterinarians to be both attentive and flexible when selecting medications and treatment regimens for the animals in their care.

In recent decades, important changes have been introduced in zoos to ensure the welfare of wild animals living in captivity. Many of these species, especially herbivores, are now housed in enclosures with access to vegetation, where they can find semi-natural habitats, interact with the environment, etc. These habitats provide favorable conditions for some parasites, such as the geohelminths, to survive and spread [9]. These parasites are difficult to control because even after successful deworming, the animals soon become infected again by ingesting parasite eggs or larvae present in the environment.

Considering the negative impact of parasitism on captive animals, the different focus of parasite control programs, the diversity of anthelmintics and the challenges of their use in wildlife, epidemiological factors that favor the spread of helminths in captive herbivores, and the need for better planning of preventive strategies and management practices for parasite control in captive animals [12–15], the goal of the present study was set: to provide an overview of the research on deworming of captive herbivorous mammals, the associated problems and the solutions sought, in order to derive recommendations for practice in the relevant institutions.

2. Materials and Methods

The information presented was obtained by searching the electronic internet databases Scopus, Web of Science, PubMed, JSTOR, Science Direct, as well as by searching Google Scholar and by following the bibliographies in published articles. Various combinations of keywords were used, including anthelmintics, benzimidazoles, captivity, deworming, herbivores, ivermectin, macrocyclic lactones, treatment and zoo. The review mainly included peer-reviewed scientific articles, written in English, dated between 1970 and 2024 and concerning captive animals.

3. Results

Most of the results concerned herbivores from the family Bovidae, followed by the families Cervidae, Equidae, Elephantidae, Camelidae and Giraffidae. The results for the families Rhinocerotidae and Ailuridae were singular. We have also included a study on kangaroos in the overview, although the animals studied were free ranging, as they are often found in zoos around the world. Herein we present the articles found in summarized form to provide a comprehensive picture of the research on helminth control in herbivores in zoological settings and the various aspects related to the control of helminthoses in these settings.

3.1. Control of Helminth Infections in Herbivores of the Bovidae Family

A case of nematode infestation in blackbucks (*Antelope cervicapra*) from Edinburgh Zoo was described by Flach and Sewell [16]. The subdominant male from a breeding group consisting of two adult males and five adult females was found in a weakened condition and died soon after. His death was attributed to a combination of his weakened condition after the group was kept overnight at a low temperature for 2–3 weeks, intermale fighting and infestation with *Camelostrongylus mentulatus*. The investigations revealed the antelopes were infected with both *C. mentulatus* and *Nematodirus spathiger*, despite routine deworming (twice a year—in spring and fall—with 7.5 mg/kg fenbendazole, administered via the supplementary feed). Fenbendazole was used to treat the infections each time, with one exception, when half of the group was administered ivermectin at a dose of 0.2 mg/kg IM by blowpipe. Control was only achieved when a different anthelmintic (oxfendazole at a dose of 4.5 mg/kg in the supplementary feed for 3 consecutive days) was administered monthly from June onwards. This control successfully reduced the number of fecal egg count (FEC) and larvae of *C. mentulatus* in the pasture, but the number of larvae of *N. spathiger* in the pasture remained unaffected, reaching a peak in mid-August. According to the authors, the high stocking density in a permanent pasture and the presence of two adult males with a breeding group of females in a small enclosure are predisposing factors for the development of these infections. They believe that the reduction in intermale stress following the death of one of the animals probably helped to control the parasite infestation, but the regular treatment from June onwards also had a profound effect, particularly in reducing the fouling of the pastures.

Mikolon et al. [17] attempted to evaluate and modify existing strongylid nematode control programs in exotic ungulates. Nine species of the subfamilies Antilopinae and Hippotraginae were observed over a two-year period to monitor the level of nematode egg shedding and the response to two different doses of fenbendazole ground in pelleted feed. Anthelmintic treatment was carried out in the base enclosures at regular intervals in fall, winter and spring. Fenbendazole (Panacur® 4% premix, Hoechst-Roussel Agrivet Co., P.O. Box 2500, Somerville, NJ 08876-1258, USA) was administered to the animals over a period of 4 days instead of the normal pelleted feed. The dosage for the fall was 114 g fenbendazole/ton of feed and was doubled to 228 g/ton of feed for the five treatments from winter to spring. In all nine ungulate species, treatment with fenbendazole was associated with a significant reduction in FECs. The response to the two anthelmintic doses was not significantly different. According to the authors, the year-round presence of infective larvae on irrigated pasture complicates strategic parasite control and frequent anthelmintic treatments (>3/year) may be required for adequate parasite control.

Mebendazole and ivermectin were evaluated for the control of gastrointestinal helminthoses in three captive gazelle species: mhorr gazelle (*Gazella dama mhorr*), Cuvier's gazelle (*Gazella cuvieri*), and dorcas gazelle (*G. dorcas*) [18]. Ivermectin was administered SC in a single dose of 0.2 mg/kg and mebendazole was given in three doses depending on the species: *G. dorcas*, 14 mg/kg; *G. cuvieri*, 6 mg/kg; and *G. dama*, 3 mg/kg orally, twice daily, for three consecutive days. The helminths detected were *Trichuris*, *Ostertagia*, *Cooperia*, *Trichostrongylus*, *Nematodirus* and *Strongyloides*. After treatment with mebendazole, nematode FECs and the number of animals shedding eggs decreased moderately. After treatment with ivermectin, the number of eggs excreted and the number of animals excreting nematode eggs decreased significantly.

Lamka et al. [19] investigated the efficacy of ivermectin in mouflons (*Ovis musimon*) with the aim of determining the optimal dose. Before treatment, larvae of *Muellerius capillaris* (heavy infection) and eggs of *Nematodirus* spp. and *Oesophagostomum* spp. (mild infection) were found in common fecal samples. Doses of ivermectin 0.20, 0.60 and 1.00 mg/kg were administered subcutaneously. Detailed helminthological examinations were performed 28–60 days after treatment and values for larvae per gram of feces and eggs per gram of feces (EPG) were determined. Based on these results, with consideration of the pathogenicity of the nematodes, the age of the experimental mouflons and cost-effectiveness of the treatment, a dose of 0.60 mg/kg body weight of ivermectin was recommended as optimal for parenteral treatment of mouflon nematodes.

Ortiz et al. [20] conducted an experiment to investigate the efficacy of mebendazole at a dose of 15–20 mg/kg against gastrointestinal nematodes in captive gazelles. The animals were divided into four groups: T1 (orally treated, directly into the mouth), T2 (orally treated, mixed into the water of a herd), T3 (orally treated, mixed into the water of an animal) and T4 (not treated). Individual fecal samples were taken before and 15 days after treatment.The average percentage reduction of egg shedding was calculated for *Nematadirus* spp., other trichostrongylids, total trichostrongylids, *Trichuris* spp. and total nematodes. Attempts to find alternative methods of administering mebendazole failed as all methods tested, including the manufacturer's recommended drenching, gave poor results. The authors comment that this lack of efficacy could be due to the following reasons: use of incorrect dosages of the drug; the fact that most pharmacokinetic studies of the drug are conducted on sheep but the results are applied to other species such as gazelles (leading to sub-therapeutic, ineffective anthelmintic dosages); the possibility that wild ruminants metabolize and excrete benzimidazoles more rapidly than domestic ones; or the development of benzimidazole resistance (BR).

In another study, Ortiz et al. [21] compared seven different methods of administering ivermectin to gazelles: subcutaneous injection, direct oral administration, administration via the individual feed, administration via the herd feed, direct oral administration of a second ivermectin formulation, administration via the individual water supply and administration via the herd water supply. The first five treatments were effective, as determined by fecal egg count reduction tests (FECRTs), and administration as a single feed or in a herd diet avoided trapping the animals with the associated risk of mortality. Oral or subcutaneous, individual or collective, direct or indirect administration was equally satisfactory for the treatment of all the parasite groups studied. Only in the case of parasite problems caused by *Nematodirus* species, direct application to individual animals was preferable.

Deworming of wild herbivores in a zoological park in Punjab was performed according to the parasitological status of the animals [22]. The drugs were administered at a higher dose (15%) to cover the losses when administered with feed. The group I animals (12 blackbucks) with single strongylid infection were treated with albendazole (Tab. Suprazole® 3 g, Ranbaxy Pvt. Ltd., Punjab, India) at a dose of 15 mg/kg $\times$ 3 days mixed with feed. The reduction in FEC was 100% on the third day after treatment and it was maintained until day 55. Albendazole thus proved to be 100% effective. The animal in group II, a ladakhi goat (*Capra ibex*) housed alone, with a mixed infestation of *Trichuris* spp. and strongylids was treated with fenbendazole (Vetfen 600 pelleted feed containing fenbendazole @ 600 mg/100 gm feed, Indian Immunologicals, Telangana, India) at 100 g for three days. The reduction of FEC in this animal was 100% on the third and fifth day after treatment for strongylids and *Trichuris* spp. respectively. This pelleted medicated feed was found to be effective in limiting the infection as no eggs were detected until 30 days after treatment. An additional benefit was also noted—it was more palatable than the other medications mixed into the feed. Group III animals, a pair of chinkaras (*Gazella bennettii*) infested with *Trichuris* spp. and strongylids, were treated with fenbendazole (Vetfen 600 pelleted feed at 600 mg/100 g feed, Indian Immunologicals) at a dose of 150 g in the feed for three days. The reduction of FEC was 100% on the third and fifth day after treatment for strongylids and *Trichuris* spp. respectively. This pelleted medicated feed was also found to be effective in limiting infection as no eggs were detected by 30 days after treatment.

The efficacy of ivermectin and levamisole against *N. spathiger* in reem gazelle (*Gazella marica*) and idmi gazelle (*Gazella gazella*) was determined by Mohammed et al. [23]. Naturally infected gazelles were divided into three groups. Groups one and two received subcutaneous doses of ivermectin (200 mg/kg) and levamisole (7.5 mg/kg), respectively. The last group was an untreated control group. The reduction in average FECs achieved by ivermectin and levamisole in the reem gazelles was 94% and 89.3%, respectively. In the idmi gazelles, the reduction was 97.2% and 96.4%, respectively. Both anthelmintics appeared to be more effective in idmi gazelles than in reem gazelles, but there was no significant difference in FECRTs in the two species.

Scimitar-horned oryx (*Oryx dammah*), roan antelope (*Hippotragus equinus*), blesbok (*Damaliscus pygargus phillipsi*) and blackbuck were treated with a single dose of 12.5 g copper oxide wire particles in bolus form [24]. Individual trichostrongylid FECs were performed before treatment, and individual post-treatment FECs were performed every 7 days for 35 days, starting 7 days after bolus administration. The average FEC reduction rates were 93% +/−16%, 98% +/−7%, 91% +/−28%, 94% +/−16% and 90% +/−13% at 7, 14, 21, 28 and 35 days post-treatment, respectively. These data demonstrate that copper oxide wire particles in bolus form are an effective method of reducing FEC in exotic artiodactylids.

Evaluation of the anthelmintic efficacy of oral fenbendazole as part of the routine twice-yearly deworming strategy in captive wild impala (*Aepyceros melampus*) was conducted in Zambia two weeks after the end of the natural rainy season [25]. The anthelmintic was administered in a non-commercial salt lick to induce ingestion by all animals. The amount of fenbendazole (Fenbenat® 4%, Opharma, Bielawa, Poland) mixed with the salt lick was estimated to deliver 5 to 8.5 mg/kg per impala daily. The amount of fenbendazole was calculated based on the estimated total body mass of the herd multiplied by 7.5 mg/kg and mixed evenly into 75% of the normal daily salt lick (assuming that some animals would ingest less and others more of the salt lick). The treatment lasted 3 days and sufficient intake of anthelmintics and salt lick by the majority of impala was estimated by observation of the game keeper. FEC was monitored one day prior to anthelmintic treatment and for a further five weeks on days 4, 8, 14, 24 and 31 after the last day of anthelmintic treatment. The effectiveness of the treatment was 90%. *Haemonchus* and *Trichostrongylus* were the predominant genera present before treatment, and *Haemonchus* was the only genus recovered from the fecal cultures after anthelmintic treatment. The study showed that the usual traditional practice of deworming captive antelopes at the end of the rainy season in Zambia is ineffective due to rapid reinfection of impalas by the high infectivity of the pastures.

Cazapal-Monteiro et al. [26] described their parasite control trials in a zoological park with many wild animals living in an area of 20 hectares divided into large parcels. Parasite control was based on the administration of anthelmintics twice a year. Despite the effectiveness of the deworming, the animals were quickly reinfected as the parcels were contaminated with infective stages of nematodes. Following the observation of high EPG levels of gastrointestinal nematodes (≥500) one month after deworming of mouflons, a study was conducted to determine the effect of adding a mixture of spores of ovicidal and nematophagous fungi (*Mucor circinelloides* and *Duddingtonia flagrans*, respectively) to concentrate feed on the risk of infection of the animals. By adding 2 × 106 parasiticidal fungal spores per kg of concentrate and administering this mixture every 2 weeks, the animals were able to maintain an elimination rate of 50–150 EPG. After one year of using this biological therapy, deworming was no longer required in the wild animals, so this method is recommended by the authors for grazing wild herbivores in captivity.

A herd of European bison (*Bison bonasus*) was dewormed by oral administration of fenbendazole (Axilur® (Vienna, Austria), granules 22%) at a dose of 3.3 g per animal twice daily for five consecutive days [27]. The anthelmintic was mixed with concentrated feed and administered in the following portions: 0.5 kg concentrated feed for calves or young animals, 1 kg for cows and 1.5 kg for bulls. In animals with ≥100 gastrointestinal nematode EPG, a fecal egg count reduction test was performed to determine the effectiveness of the treatment. In addition, a PCR analysis was performed to identify the parasite species. The FECRT showed that the reduction of strongylid EPG in the bison herd studied was 87%, indicating a reduced efficacy of fenbendazole on gastrointestinal strongylids, mainly *Haemonchus contortus*.

According to Lahat et al. [28], wild animals in captive breeding programs are often treated with anthelmintics, which is effective from a health management perspective, but could prevent captive animals from developing effective immunity against parasites they might encounter when reintroduced to their original geographic range. Researchers conducted a study to describe the dynamics of parasite infections in captive Cuvier's gazelles that were not treated with anthelmintics for two years and to evaluate the factors associated with their fecal egg shedding. The eggs in the feces were counted and classified as strongylid-like, *Nematodirus* sp., or *Trichuris* sp. Fecal egg excretion for the three parasite groups did not vary significantly over the duration of the study. Only rainfall had a positive effect on egg shedding for all parasites, while inbreeding was positively associated with the number of strongylid-like parasites. These results suggest an equilibrium between hosts and parasites when there was no treatment during the study. For this reason, the authors recommend avoiding treatment with anthelmintics as a systematic prophylactic method in captive animals and replacing it with systematic coprological and clinical monitoring and targeted treatment in case of a significant increase in FECs.

The death of a European bison from a wildlife park due to haemonchosis despite frequent anthelmintic treatment of the herd with fenbendazole and doramectin prompted an investigation of various ruminant species inhabiting the park for resistance to anthelmintics [29]. Following coproscopic examination, fecal larval cultures were prepared and *H. contortus*-positive cultures were analyzed for genetic polymorphisms associated with BR. It was found that in some samples from bison and mouflons the frequency of the resistance-associated single nucleotide polymorphism at codon 200 of the β-tubulin isotype 1 gene was 100%. Possible resistance to macrocyclic lactones was also indicated. According to Springer et al. [29], the detection of nematodes resistant to anthelmintics in these animals is of particular concern with regard to their planned reintroduction into the wild. They point out that care should be taken to avoid underdosing or unnecessarily frequent treatments that favor the development of resistance to anthelmintics. As resistance is not reversible, veterinarians dealing with such animal collections should be aware of sustainable strategies to maintain the efficacy of anthelmintics for as long as possible.

The efficacy of deworming measures against gastrointestinal nematodes in captive European bison was investigated by Galazka et al. [30]. The animals were treated as follows: with albendazole (10 mg/kg PO; Valbazen® 10%, Zoetis, Zaventem, Belgium) or fenbendazole (10 mg/kg PO; Fenbenat 40 mg/g®, Vetos-Farma, Bielawa, Poland) for five consecutive days; with ivermectin (0.3 mg/kg PO; Iwermektyna Vetos-Farma 0.6 g/100 g®, Vetos-Farma, Bielawa, Poland), administered once; or with levamisole (7.5 mg/kg PO; Levamol 5%®, Vetoquinol Biowet, Wielkopolski, Poland), administered once. In some facilities the anthelmintics were mixed with the concentrated feed and administered individually. In others, the animals were divided into groups based on estimated body weight and the medication was administered mixed into pelleted feed. One day before deworming, the animals were not given concentrated feed. In all cases, deworming with albendazole, fenbendazole and ivermectin proved ineffective against strongylids and *Trichuris* sp. The results of the FECRT ranged from 37.2 to 99.6% for albendazole; values of >95% were found for fenbendazole and 63.2–97.5 for ivermectin. According to the authors, these results are not satisfactory.

3.2. Control of Helminth Infections in Herbivores of the Cervidae Family

Presidente et al. [31] observed an outbreak of dictyocaulosis in a herd of captive black-tailed deer (*Odocoileus hemionus*). After treatment with levamisole hydrochloride (16 mg/kg) administered as a leachate solution, there was a transient decrease in excretion of *Dictyocaulus viviparus* larvae in the feces. Lungworm larvae were not recovered in the feces 6 days after administration of cambendazole at doses of 40 and 50 mg/kg but were recovered between 15 and 23 days after treatment. Larval excretion in feces increased when fawns were kept on an intensively used contaminated grass pasture. The deteriorating physical condition of the fawns required additional treatment with cambendazole and relocation to a forest where reinfection by ingestion of larvae was minimized. Repeated treatment with cambendazole 3 weeks after the first treatment resulted in complete elimination of the infection, which according to the authors was due to the elimination of the immature lungworms that were not affected by the first treatment.

Goossens et al. [32] conducted a 12-month survey of gastrointestinal helminth infections in cervids kept in two Belgian zoos—the Antwerp Zoo and the Planckendael Zoo in Mechelen. Both locations differed considerably in the type of enclosures, dung removal practices and the use of anthelmintics. Nematode eggs were found in all herds at both locations, but the extent of infection was very different. While nematode eggs were rarely found at site 1 (the small urban zoo), the deer in most herds at site 2 (the animal park) were constantly shedding eggs. According to the authors, the daily dung removal from the small enclosures and stables at the zoo eliminates eggs and thus also the infectious larvae. In contrast, the larger, muddy, and grassy enclosures of the animal park are more favorable for the development of infective larval stages, which explains the frequent occurrence of gastrointestinal nematodes. Routine anthelmintic treatment with fenbendazole in April and July limited egg shedding, but the treatment appeared to have little effect as reinfection quickly occurred. Egg shedding decreased in winter, indicating a small adult nematode population. The FEC for *Trichuris* spp. peaked in February in European elk (*Alces alces*), but an adult male reindeer (*Rangifer tarandus*) housed in the same enclosure did not shed *Trichuris* spp. eggs throughout the study period. The authors concluded that infestation with infective larvae in the pastures is the main source of infection and that control programs applied to livestock, such as pasture rotation and early season treatment, can also be used to prevent nematode infections in captive deer.

Fathima et al. [33] investigated the anthelmintic efficacy of albendazole and ivermectin in captive spotted deer (*Axis axis*) from two zoos in India. Both drugs were administered orally, mixed with concentrated feed, ivermectin at a dose of 0.2 mg/kg and albendazole at a dose of 5 mg/kg. The FECRT showed 100% susceptibility to albendazole and 97% efficacy of ivermectin, indicating low resistance.

Two different formulations containing a mixture of spores of the filamentous fungi *M. circinelloides* and *D. flagrans* were tested against trichostrongylids in zoo wapitis (*Cervus canadensis*) dewormed with fenbendazole [34]. One approach (sprayed-on pellets) involved spraying fungal spores onto the food pellets shortly before ingestion for 10 months, and the other (formulated pellets) involved administration of industrially produced pellets containing the spores over the same time period. Wapitis treated with fenbendazole (Panacur® 10, MSD Animal Health, Spain or Laboratorios Syva, Leon, Spain) at a dose of 5 mg/kg administered quarterly without receiving spores during a 10-month interval were considered as controls. The effect of these strategies was evaluated by analyzing the FEC of trichostronylids. Despite the success of fenbendazole, levels of trichostrongylid egg output increased above 300 EPG four months later. A significant EPG reduction was recorded with the administration of spores: 69% with the sprayed pellets and 71% with the industrially spore-enriched pellets. No unfavorable effects were observed in the wapitis ingesting the spores. It is concluded that ingestion of a mixture of the tested spores every two days has a positive long-term effect in controlling trichostrongylid infections in captive wildlife.

Luginbühl et al. [15] presented a study on the keeping of Swiss reindeer in captivity (on farms or in zoos). The survey showed that anthelmintics were used in every herd: all zoos used fenbendazole in pellets or in powder form; the private herds used agents such as fenbendazole, moxidectin, doramectin, monepantel or a combination of levamisole and triclabendazole; in one herd, toltrazuril was administered once a year. However, the reindeer harbored a variety of endoparasites, with the prevalence of infection in this study population being 73%. Differences in the prevalence of infection were observed in zoos and private farms. Reindeer in zoos appear to be less frequently infected with nematodes, which the authors explain in several ways: in zoos there are fewer calves and thus fewer reservoirs of infection; reindeer in private husbandry have more pastures in their enclosure, on which they also feed and which are an ideal place for the parasites to complete their life cycle and (re)infect their hosts; reindeer without pastures may spend less time eating from the ground, where they also defecate, and therefore have a lower chance of becoming (re)infected; in zoos, part or all of the enclosures are cleaned more frequently than in private keepings, resulting in a lower parasite load.

The efficacy of anthelmintics against gastrointestinal nematodes in cervids was evaluated by Sahu et al. [35]. Spotted deer, sambar (*Rusa unicolor*), and barking deer (*Muntiacus muntjak*) with an egg count of more than 150 EPG were selected for the study. The animals were randomly divided into an untreated control group (I) and two treatment groups, i.e., ivermectin (II) and fenbendazole (III). The animals were treated with anthelmintics according to the manufacturer's recommended dose as part of the routine three-month deworming program. Both drugs were administered orally, mixed with concentrated feed: ivermectin (Bolus Neomac®, Intas Pharmaceuticals Ltd., Ahmedabad, India) at a dose of 0.2 mg/kg and fenbendazole (Bolus Panacur® 1.5 VET, Intervet India Pvt. Ltd., Thane, Maharashtra, India) at a dose of 7.5 mg/kg. FECRT showed 97% efficacy for ivermectin and constantly reduced egg excretion by more than 95%. Fenbendazole was found to be 96.15% effective against nematodes at day 14 post-treatment. No significant difference was found in the efficacy of ivermectin and fenbendazole. According to the authors, both anthelmintics can therefore be used in a strategic control program against gastrointestinal nematodes in cervids.

3.3. Control of Helminth Infections in Herbivores of the Equidae Family

Lia et al. [36] investigated the efficacy of medicated feed pellets to control intestinal strongyles in captive zebras (*Equus quagga*). From day 0 to day 9, a feed formulation containing 10 mg ivermectin per kg of pellets (UNIFEED, Veronesi, Verona, Italia) was administered to the animals by dividing it into 10 portions of 10 kg each (i.e., a total of 100 mg ivermectin) and placed in the paddock for all 30 zebras. This procedure allowed a theoretical daily administration of 1 g ivermectin for 30 zebras (i.e., about 0.118 mg ivermectin/kg/day) during the entire 10 days of treatment. The estimated daily dose was slightly higher than that recommended for domestic horses to avoid underdosing in animals consuming smaller amounts of ivermectin-containing feed. The drug showed 100% efficacy up to 78 days after treatment, with one exception related to the fact that some animals consumed a lower amount of ivermectin-containing daily ration than that required for long-lasting efficacy. This could be a consequence of the behavior of zebras in captivity (they eat together in the same manger, and the strict hierarchy and behavior of dominant animals eating before the others could result in some animals ingesting lower amounts of ivermectin). According to Lia et al. [36], this could increase selection pressure for drug-resistant populations due to underdosing. To avoid this risk, they recommended individual feeding of captive equids and concluded that macrocyclic lactones are currently the most effective drugs for controlling equine strongyles, although there have been recent reports of their reduced efficacy.

Orally administered ivermectin at a dose of 400 μg/kg was used to treat 20 ponies (*Equus ferus caballus*) with cyathostome and pinworm infections [37]. It was highly effective in cyathostome infection, however adult *Oxyuris equi* worms were detected in 6 horses after treatment. The authors comment that anthelmintic treatment with macrocyclic lactones in recent years in the USA did not appear to show the expected efficacy against pinworms in horses (*O. equi*). This was the first European study to demonstrate resistance of *O. equi* to macrocyclic lactones in ponies.

Arias et al. [38] conducted a study to determine the positive effect of including biological methods in parasite control programs for equids in zoological parks. Two trials were designed for zebras, donkeys (*Equus asinus*) and African wild asses (*E. africanus asinus*)—the first consisting of chemotherapy only (ivermectin plus praziquantel), and the second the administration of chemotherapy and chlamydospores of the nematophagous fungus *Arthrobotrys (Duddingtonia) flagrans*. In the first trial, 100% FEC reduction was achieved in all animals 15 days after treatment, and the egg reappearance period (ERP) was 2–3 months. In the second trial, FEC reduction was also 100% in the three species and ERPs were 3 months in the European donkeys, 4 months in the Africans and 6 months in the zebras. This study has shown that the introduction of chlamydospores of a nematophagous fungus such as *A. flagrans* is very promising for the reduction of infective stages of strongyles infesting captive animals.

The integrated control of strongyles in captive wild equids (zebras, European donkeys and African wild asses) was investigated over a period of three years [34]. In the zoo, feces were removed daily before visitors entered the park, but the captive equids were always housed in the same area as rotation was not possible. Prior to the trial, the FEC was monitored monthly and anthelmintic therapy was recommended if the number of strongylid eggs in one gram of feces exceeded 400. During the trial, parasite control consisted of deworming with Equi-max® (Virbac, Barcelona, Spain) containing ivermectin + praziquantel at a dose of 1.07 g/100 kg body weight); in addition, every two days the equids received commercial feed pellets containing an industrially produced mixture of 104–105 spores of the fungi *M. circinelloides* (ovicidal activity) + *D. flagrans* (larvicidal activity) per kg meal (approximate amount of 2.5 kg pellets individually per animal). During the experiment, four anthelmintic treatments were administered: three times in the first 2 years and one further treatment in the last year. Values of 96–100% for FEC reduction and 75–100% for positive horses were achieved. The ERP ranged from eight to twenty-eight weeks, and the time since the last deworming ranged from four to eighteen months, with an increasing trend continuing to the end of the study period. No side effects were observed in any of the equines. According to the authors, these data indicate the success of the experiment. They discuss the positive effects of using fungi for the biological control of strongylids which, besides reducing the frequency of treatment of the animals, include the reduction of development and presence of L3 strongylids in the soil and thus reduction of ecotoxicity of anthelmintics on organisms responsible for soil enrichment, such as the dung beetles necessary for the decomposition of manure. Palomero et al. [34] conclude that the method of including filamentous fungi in the diet together with anthelmintic deworming is a novel and sustainable strategy for the development of strongylid control programs in captive wild equids.

The efficacy of ivermectin against nematodes in captive Przewalski's horses (*Equus ferus przewalskii*) after ten years of annual treatment was investigated by Tang et al. [5]. An oral paste of ivermectin (Beijing Wanfeng Pharmaceutical Laser Target Designator, Beijing 100193, China; 2 mg/g) was mixed with cornmeal and fed to all horses at a dose of 100 μg/kg. The number of eggs per gram of feces usually increased dramatically 1–2 days after treatment and gradually decreased to 0.0 within 15 days. According to the authors, this study is an example of a successful program to control parasitic nematodes in reintroduced animals over a decade using a single dewormer with low treatment frequency. They explain that low treatment frequency and inadequate fecal management are likely to slow the development of anthelmintic resistance due to the presence of large numbers of eggs and free-living larvae of the susceptible genotype in the pasture, also known as refugia population. An increase in the refugia population could even restore the lost efficacy of anthelmintics.

Kuzmina et al. [39] analyzed the manifestations of BR in strongylids in plains zebras and Grevy's zebras (*Equus grevyi*) kept under semi-free conditions. Regular anthelmintic treatments were carried out twice a year—in spring before the start of the grazing season and in fall at the end of the grazing season—but the animals were not treated with anthelmintics for four months prior to this study. The most heavily infected animals with EPG > 150 (n = 90) were selected and dewormed with albendazole (Albendazole-10%® ZooVetPromSnab, Ukraine) at a dose of 0.75 g per 10 kg body weight. As the deworming of the wild equids was only possible by adding the anthelmintic mixed with feed (oat grain) to the trough, the dosage of the drug was increased by 10% for each animal to avoid underdosing related to the distribution of the drug in the trough. The efficacy of the anthelmintic treatments in 2019 was low: 69.4% in plains zebras and 72.7% in Grévy's zebras. Analysis of long-term data (2009–2019) showed a decline in the efficacy of benzimidazoles against strongylids from 97.6% in 2009 to <75% in 2019. The analysis of the multi-year (2009–2019) EPG values showed that in all equids treated twice a year or less, the first signs of BR appeared in the years 2010–2012. According to the authors, this trend is an indicator that frequent deworming is not a major factor in the development of BR. They assume that underdosing of anthelmintics is the main factor for the development and spread of BR in strongylids in all equids kept in the Askania Nova Reserve, especially in zebras. Kuzmina et al. [39] note that it is almost impossible to precisely control the dosage of anthelmintics when deworming wild equids. Normally, the anthelmintics are given to the animals mixed with the feed, but most wild equids, especially zebras, are reluctant to eat feed containing the anthelmintics; therefore, it is very likely that they receive a lower dosage of the drugs.

Obviously, different husbandry and deworming programs are for a key factor in whether resistance to anthelmintics develops. For example, in two Romanian zoos—Targu-Mures and Turda—resistance of strongylids to benzimidazoles was found in horses and ponies, while in a third zoo—Baia-Mare—the efficacy of benzimidazoles was good in all equine species [40].

3.4. Control of Helminth Infections in Herbivores of the Elephantidae Family

Strongylosis was diagnosed in elephants with clinical symptoms such as loss of appetite of varying degrees, pallor of the conjunctiva and discharge of foul-smelling, slightly diarrhea-like feces [41]. After treatment with oral albendazole (Kalbend® (Peenya, Bangalore) 1.5 g—at 5 mg/kg body weight), the animals recovered completely on the seventh day without any symptomatic treatment. The therapy lowered the average pre-therapeutic EPG from 700 and 671.4 to 78.57 and 50, for the two farms respectively. Monitoring of the elephants for up to four weeks after therapy revealed a normal state of health with no helminth eggs in the feces. According to the authors, this is an indication of the efficacy of Kalbend® in the treatment of strongylosis in elephants.

African elephants (*Loxodonta africana*) are susceptible to a variety of parasites, which are often treated with the broad-spectrum antiparasitic ivermectin based on empirical evidence. Gandolf et al. [42] conducted several studies with the objectives of: (1) measurement of ivermectin plasma levels after administration of 0.1 mg/kg PO, (2) comparison of ivermectin plasma levels after administration with regular or restricted feed rations, (3) measurement of ivermectin excretion in feces, and (4) use of these results to establish dosing recommendations for this species. Based on their results, the authors believe that that administration of 0.2–0.4 mg/kg ivermectin PO should be suitable for elimination of many types of parasites in elephants and could minimize development of parasite resistance.

Specific schemes of ivermectin application in elephants and results of the treatment are presented in another study [43]. Ten animals naturally infected with microfilariae were divided into 2 groups and treated with ivermectin on day 0 (group 1) or on day 0 and 15 (group 2). Five elephants that were not infected with microfilariae formed the control group. Ivermectin 10 mg/mL (% *w*/*v*) was administered SC at a dose of 1 mL/100 kg body weight, which was half the normally recommended dosage. Blood samples were taken from the 15 animals on days 0, 15, 30, 60, 90 and 120 to determine the microfiolaria titres and evaluate the blood parameters. Fecal egg counts were performed on all 15 elephants on the same days. The peripheral blood of the experimental animals was cleared of all microfilariae on day 15 after treatment and no infestation with microfilariae was observed until day 90. Both treated groups were reinfected by day 120. The average values of nematode EPG decreased after the injection of ivermectin in the treated groups. The authors concluded that a single dose of ivermectin (1%) administered SC not only reduced the density of microfilariae in the peripheral blood of elephants, but also significantly reduced the number of gastrointestinal nematodes. A single administration of ivermectin (1%) at half the recommended dose is effective in eliminating microfilariae for up to three months. Therefore, the drug should be administered to the elephants four times a year.

The review by Pathak and Chabra [44] mentions various drugs and regimens for deworming Indian elephants (*Elephas maximus indicus*): hexachlorophene (Distodin®, Mumbai, India) at a dosage of 10 mg/kg orally was 100% effective against amphistomes; triclabendazole at a dosage of 9 mg/kg (up to a maximum of 7200 mg/animal) and oxyclozanide at a dosage of 7.5 mg/kg (up to a maximum of 6.8 g/animal) were 100 and 72.16% effective against fascioliasis; oxyclozanide bolus at a dose of 5 mg/kg proved effective against amphistomes and/or *Fasciola*; oxyclozanide (Zanil®, MSD Animal Health UK Limited, Walton, UK) at a dose of 3.4 mg/kg as a single dose in the feed resulted in elimination of tapeworm segments and alleviation of symptoms such as anorexia, loss of condition, eating of mud and grit, and diarrhea. According to the study, other drugs that could be tried against cestodes are niclosamide (75–100 mg/kg orally), hexachlorophene (10 mg/kg orally), mansonil (5 mg/kg) and praziquantel (2.5–4 mg/kg). A variety of anthelmintics have been used to treat gastrointestinal nematodiasis, including tetramisole, thiabendazole, methyridine, thiophanate and oxybendazole, with varying degrees of success. A study on the comparative efficacy of 6 anthelmintics against strongylosis showed that mebendazole at a dosage of 3–4 mg/kg, levamisole at a dosage of 3 mg/kg and morantel tartrate at a dosage of 5 mg/kg body weight were 100% effective. Fenbendazole as a single oral treatment of 5 mg/kg body weight or 2 doses of 50 g was effective against murshidiasis in 200 elephants and 12 g in 200 mL water in 2 divided doses 3 days apart—against trichostrongyle infections. Fenbendazole at a dose of 5 mg/kg was found to be equally effective against strongyles and amphistomes, while a similar dose of albendazole resulted in complete cure of strongylosis.

Abeysinghe et al. [45] investigated the prevalence and abundance of gastrointestinal strongylids in captive Asian elephants under two parasite management regimens and compared them with those in wild elephants. Privately owned elephants that were dewormed every 3 months had significantly fewer parasites than elephants that were dewormed every 6 months or "as needed". Elephants receiving anthelmintics "as needed" had a similar parasite load to elephants treated on a 6-month schedule or wild elephants. According to the authors, the variance in parasite infection parameters is probably due primarily to differences in anthelmintic treatment and secondarily to husbandry practices. Abeysinghe et al. [45] concluded that controlling gastrointestinal helminths in captive elephants based on natural immunity is preferable to the potential negative consequences of intensive long-term drug use. They believe that boosting the immunity of captive elephants through adequate nutrition, hygiene and minimizing stress, together with regular fecal examinations and treatment of individuals with an above average parasite burden, is a better approach to elephant parasite control.

Captive Asian elephants diagnosed with helminth infection (strongylid nematodes, *Strongyloides* spp., *Anoplocephala* spp. and *Fasciola* spp.) with a high prevalence (89.12%) were treated with a single dose of 3 mg/kg febantel [46]. The percentage of FECs reduction was 67.82% and 49.32% on day 7 and 28 after treatment, respectively. The increase in parasite eggs within 30 days after deworming showed that the febantel was not sufficient to eliminate all gastrointestinal parasites in the affected animals.

Baishya et al. [47] dewormed an Indian elephant infected with *Fasiola jacksoni*, amphistomes, strongylids and *Strongyloides* with two oral drugs: closantel (Zenvet bolus®, Gurugram, India)—10 g total dose repeated after 15 days against *F. jacksoni* and amphistomes and fenbendazole (Fentas 3 g bolus®, Intas Pharmaceuticals Ltd., Alhamabad, India) × 4 repeated after 15 days against strongylids. The following treatment was carried out together with anthelmintics: Feroliv Fe bolus—4 boluses twice daily orally for 15 days, Minerex Gold bolus—2 boluses twice daily for 1 month, Tribivet injection—20 mL daily by IM route on alternate days for 5 occasions. The animal was re-examined for the presence of helminth eggs after 20 days of treatment. No more eggs were found, indicating successful elimination of the mixed parasite infestation.

3.5. Control of Helminth Infections in Herbivores of the Camelidae Family

Burkholder et al. [48] investigated the plasma levels of ivermectin by high-performance liquid chromatography in five llamas (*Lama glama*) after a single injection of 200 µg/kg SC. Ivermectin levels were not detectable in plasma samples taken up to 4 weeks after injection, indicating that the dosage used was insufficient to achieve therapeutic concentrations in this species.

Eo et al. [49] described their experience of deworming captive dromedary camels (*Camelus dromedarius*). One adult (13 years old) and two young (3–4 years old) male camels developed anorexia and chronic diarrhea for 2 weeks. Examination revealed infection with *Trichuris* spp. and fenbendazole was administered orally as a suspension; this was repeated twice at 3-week intervals. A high initial dose (20 mg/kg) was followed by administration of the recommended dose (10 mg/kg). Many adult whipworms were excreted in the feces over 3 days, starting the day after the first treatment. The young camels gradually recovered but the adult animal developed bloody, mucoid diarrhea and died days after treatment. A similar case was reported in which an infected adult camel also died despite treatment [50].

According to a survey of worm control practices in farmed alpacas (*Lama pacos*), the most commonly used anthelmintics were macrocyclic lactones, monepantel, benzimidazoles, levamisole, closantel and their combinations, and they were usually administered at the dose recommended for sheep [51]. A combination of levamisole, closantel, albendazole and abamectin was the most effective dewormer, followed by single drugs including monepantel, moxidectin, closantel, fenbendazole and ivermectin. *Haemonchus* spp. were the most commonly resistant nematodes, followed by *Trichostrongylus* spp., *C. mentulatus*, *Ostertagia ostertagi* and *Cooperia* spp.

Dr. Pamela Walkerdiscussed various aspects related to gastrointestinal parasites in camelids, including when it is necessary to deworm these animals, whether group or individual deworming is more appropriate, what tests should accompany the antiparasitic treatment, the relationship between the treatment and type of parasite, etc. [52]. Deworming of camelids can be done, as a general guideline, after a series of fecal analyses. If the number of strongylid eggs in one gram of feces is less than 200, the deworming program applied (husbandry/medication) can be considered to still be effective. If this number starts to rise, then it could indicate a problem. Dr. Walker recommends withholding the animal's food overnight when using oral anthelmintics. This slows the flow of gastrointestinal contents and allows an increase in the time the drug is in contact with the parasite. Another way to increase the efficacy of a medicine is to repeat the intake at intervals of 12 h, which again increases the duration of contact between the medication and the parasite. This works best with fenbendazole but should not be done with albendazole. Dr. Walker [52] described the drugs most used as anthelmintics in camelids, giving the specific doses, concentrations and methods of administration, and accompanied them with valuable comments, precautions and guidelines.

3.6. Studies on the Control of Helminth Infections in Herbivores from Different Families

Goossens et al. [53] investigated the efficacy of fenbendazole (Panacur®; Intervet) in Arabian oryx (*Oryx leucoryx*), scimitar-horned oryx, slender-horned gazelles (*Gazella leptoceros*), Soay sheep (*Ovis aries aries soay*), Alpine ibex (*Capra ibex ibex*), red deer (*Cervus elaphus*) and Nelson's elk (*Cervus elaphus nelsoni*), when administered with the feed at a dose of 7.5 mg/kg for three consecutive days. The animals were reluctant to consume the fenbendazole powder mixed with the feed pellets, and each animal ate about 90 to 94 percent of the administered drug. The medicine administered in this way was highly effective in scimitar-horned oryx, slender-horned gazelles, Soay sheep, red deer and Nelson's elk, but lower efficacy (<90%) was observed in Arabian oryx and ibex. The authors discussed various possible reasons for this and finally concluded that BR could develop in the nematodes infecting Arabian oryx and ibex and suggested macrocyclic lactones as a replacement for benzimidazoles for these animals.

Goossens et al. [54] carried out a 12-month study of the gastrointestinal helminths of antelopes, gazelles and giraffes kept in two Belgian zoos—Antwerp Zoo and Animal Park Planckendael. During the study, no routine anthelmintic treatment was carried out at Antwerp Zoo, as there had been no suspicion of helminthosis in the previous 5 years. At the Animal Park Planckendael clinical signs of gastroenteritis were regularly observed over the previous 5 years and were often attributed to helminth infections. Routine helminth control at this site consisted of administering fenbendazole (Panacur®, Intervet, Vienna, Austria) in the feed to all ruminants at a dose of 7.5 mg/kg for three consecutive days twice a year. The herds of Arabian oryx, scimitar-horned oryx and gazelles received an additional 3-day fenbendazole treatment when they were stalled for the winter, as clinical helminthosis had been suspected during stabling in previous years. The level of nematode infections was extremely low at Antwerp Zoo, which the authors believe is probably due to the lack of grazing and daily dung removal. In the Planckendael park, significant differences were found in the infection rate of various herds, mainly due to the housing conditions and to a lesser extent the susceptibility of the individual species or animals. The authors concluded that the identification of highly infected ungulates and knowledge of the seasonal variation of their helminths can make an important contribution to well-adapted species-specific management and helminth control programs.

Three parasite control programs were evaluated in three consecutive years in different captive wild ruminants [55]. In the first year, a biannual spring-summer treatment was given with fenbendazole at a dose of 7.5 mg/kg, PO, for three days. The next year, a treatment program was carried out at the beginning of the season with 3 administrations of fenbendazole at the same dosage, 3 weeks apart. In the third year, a treatment program with ivermectin (0.2 mg/kg, PO, for three days), administered three times at 5-week intervals, was evaluated early in the season. In the spring-summer regime, FECs remained low for the first five months, but from September onwards they slowly increased to a significant level in all seven herds. The early season fenbendazole program resulted in near zero FEC throughout the year in four herds, but significant egg shedding was observed in Arabian oryx, scimitar-horned oryx and Soay sheep from August onwards. The early-season ivermectin program resulted in very low to no egg shedding in gazelles, adult Soay sheep, ibex, red deer and Nelson's elk throughout the grazing season, but could not prevent high egg shedding in Arabian oryx and scimitar-horned oryx in October. According to the authors, the failure of the treatment regimens in some herds can be explained by a high contamination of the grass areas with infective larvae/eggs in the previous year or before the first treatment.

Fagiolini et al. [56] investigated gastrointestinal parasites in mammals in two zoological gardens with different husbandry practices and parasite control. These were the Zoo Safari of Fasano (140 hectares; mainly open natural enclosures; not always easy dung removal; twice-yearly anthelmintic treatment on a rotational basis; in case of diarrhea and positive parasite feces the animals are treated accordingly and subsequently checked) and the Giardino Zoologico of Pistoia (7.5 hectares; indoor and outdoor enclosures; daily dung and weekly substrate removal; monthly fecal analyses; targeted treatment of infected animals and weekly fecal analyses after the treatment period). Significant differences were found in the frequency of helminth infections in both zoos: all samples from the first zoo were positive while those from the second zoo were negative for gastrointestinal strongylids; the frequency of helminthoses in perissodactyls and artiodactyls was significantly higher in the first zoo; and all Bactrian camels (*Camelus bactrianus*) from the first zoo were positive for gastrointestinal strongylids, while those from the second zoo were positive for *Trichuris* spp.. Gastrointestinal strongylids were also found in a high percentage in other herbivores from the first zoo. The authors concluded that cleaning and removal of the dung, together with routine analysis of feces for parasites and selective treatments carried out at the Giardino Zoologico of Pistoia, were more effective measures to control the nematode infections.

Spotted deer, sambar, barking deer and four-horned antelope (*Tetracerus quadricornis*) received Neozide plus suspension (oxyclozanide—6% *w*/*v* + levamisole—3% *w*/*v*, INTAS Pharmaceuticals) mixed into the feed at a dosage of 15 mL/head for spotted deer, 50 mL/head for sambar and 5 mL/head for barking deer and four-horned antelope [57]. The anthelmintic reduced the FEC to zero, resulting in 100% efficacy on day 10 post-treatment in sambar. Recurrence of infection was observed on day 21 post-treatment in sambar and spotted deer, resulting in a decrease in anthelmintic efficacy, while in barking deer and four-horned antelope, recurrence was observed after day 45 of treatment. According to the authors, the impossibility of completely eliminating the parasite load in herbivores is a consequence of the stress and close proximity of the animals, as well as mass deworming, where it is difficult to determine whether the animals have been exposed to the drug.

Intestinal parasites of the Alpine ibex, the chamois (*Rupicapra rupicapra*), the European mouflon, the fallow deer (*Dama dama*), the red deer, the alpaca, the Bactrian camel, chapman's zebra (*Equus quagga chapmani*), guanaco (*Lama guanicoe*), red lechwe antelope (*Kobus leche*) and reticulated giraffe (*Giraffa camelopardalis reticulata*) were observed over a period of eight years [58]. In the case of helminthoses, the animals were treated with doramectin and fenbendazole one week after diagnosis and the result was evaluated 14 days later. The results showed that gastrointestinal parasites were common and, in some cases, highly prevalent. Regular monitoring and targeted treatment led to a reduction in deaths from parasite infestation, which used to be very common. Kvapil et al. [58] concluded that the quarantine period of 30 days, including coprological examination, deworming treatment and monitoring of treatment efficacy, is insufficient and did not prevent the spread of parasitic infections. This suggests that the duration of quarantine, disinfection protocols and deworming programs need to be re-evaluated. The possibility of mechanical transmission of eggs must be prevented, as the usual disinfection barriers in quarantine aim at preventing the bacterial spread of infections but are unable to adequately control resistant parasite eggs. The timing of the coprological examination, treatment and control examination is also important, as the times at which certain parasites shed their eggs vary greatly. Regular coprological examinations four times a year seem to be sufficient to control the parasite load in most animals but must be individually adapted to the sensitive species.

Take et al. [59] evaluated commercial antiparasitic molecules with the aim of optimizing the zoo therapeutic protocol. Artiodactyla (giraffes, addax, Cuvier's gazelles, Thomson's gazelles) infested with gastrointestinal nematodes were treated as a group with fenbendazole oral suspension, 7.5 mg/kg, once daily, for 3 consecutive days, while Perissodactyla (Grant's zebras) were treated with fenbendazole oral suspension, 10 mg/kg, once daily, for 3 consecutive days. Gastrointestinal nematodes in Skimitar oryx were treated individually with ivermectin, 0.2 mg/kg once by remote injection. The efficacy of the drug on the 7th day after treatment was 66.66% in Artiodactyla and 100% in Perissodactyla. According to the authors, many factors could be responsible for these results, but the main reason was the partial consumption of the drug dose and/or the dominance of individual animals over the rest, resulting in excessive consumption in some and non-consumption in others. In systemically treated animals, such as oryxes, the parasite detection was negative, which is probably due to the administration of the entire dose. However, this type of treatment is only possible with a small number of individuals or animals housed separately in cages.

The efficacy of two ivermectin prophylactic treatments in zoo mammals was verified by Zanzani et al. [60]. Herbivores were treated twice a year with ivermectin in a feed formulation (medicated feed containing 1.7 g/ton ivermectin) daily for 30 days in March and November. Fecal samples were examined in June–July and October, and nematode infections were found with *Nematodirus* spp., *Capillaria* spp., *Trichuris* spp. and *Parascaris* spp. more frequently than Strongylida. According to the authors, possible reasons for this fact could include: (1) During the 30-day period of prophylactic ivermectin treatment, free-living Strongylida stages did not find appropriate environmental conditions to survive and reinfect the hosts, even if the prophylactic treatment was interrupted, while the eggs of *Nematodirus* spp., *Capillaria* spp., *Trichuris* spp. and *Parascaris* spp., which all have a higher environmental resistance, probably persisted longer in the soil. (2) The effects of prophylactic treatments may depend on the host species; Elephantidae, Hippopotamidae, Macropodidae, Rhinocerotidae and Tapiridae were not suitable hosts for *Nematodirus* spp., *Capillaria* spp. and *Trichuris* spp. (3) The effects could also depend on the individual susceptibility of the host to different classes of substances. For example, the detoxification capacity of xenobiotics is more pronounced in goats than in sheep due to their feeding behavior. The same could apply to herbivores housed in faunistic parks. In the wild, Giraffidae are considered general browsers and are probably more exposed to plant toxins. Zanzani et al. [60] concluded that the frequency and dose of prophylactic treatments in zoo herbivores should be improved according to taxonomic groups of hosts and parasites.

3.7. Studies on the Control of Helminth Infections in Herbivores of the Families Giraffidae, Ailuridae, Macropodidae and Rhinocerotidae

A case of persistent haemonchosis in a young male giraffe was described by Garretson et al. [61]. Upon arrival at Loxa hatchee, Florida, the animal's feces were normal in appearance, but during quarantine it was diagnosed with *Haemonchus* sp. infection. The giraffe was treated with a single oral dose of ivermectin (Eqvalan®, 10 mg/mL, Merial Limited, Duluth, GA 30096-4640, USA) at 0.2 mg/kg in combination with fenbendazole (Panacur® Suspension 10%, DPT Laboratories, San Antonio, TX 78215, USA) at 5.0 mg/kg once daily PO for 3 days. Two weeks later, an approximate 80% reduction in egg numbers was found and the animal was treated with an oral dose of moxidectin (Quest 2% gel, Fort Dodge Animal Health, Fort Dodge, IA 50501, USA) at 0.4 mg/kg. No eggs were found in fecal examinations 1 and 3 weeks after treatment and the giraffe was introduced to the resident giraffe population. Seven weeks later, this giraffe presented with diarrhea and was diagnosed with an extremely high FEC of *Haemonchus* sp., with resistance to benzimidazoles, imidazothiazoles and macrocyclic lactones. The giraffe was treated with a topical dose of moxidectin (Cydectin®, 5 mg/mL, Fort Dodge Animal Health, Overland Park, KS, USA) at 0.5 mg/kg in combination with an oral dose of fenbendazole (Panacur® granules 22.2%, Pantheon Inc, Toronto, ON, Canada) at 6.8 mg/kg once daily for 3 days, followed by an oral dose of ivermectin (Eqvalan® (Paramus, NJ, USA), 10 mg/mL) at 0.2 mg/kg 15 days later. A second topical dose of moxidectin (Cydectin®, 5 mg/mL) at 0.5 mg/kg was administered two weeks later. This treatment resulted in resolution of the diarrhea and a negative simple flotation test two weeks later. However, within 2 months, the giraffe's EPG was 11,900 and the animal was then treated with a topical dose of moxidectin (Cydectin®, 5 mg/mL) at 1.2 mg/kg in combination with 6 g of copper oxide wire particles (COWP, Copasure® 12.5-g capsules, Animax Ltd., Stanton, UK) and removed from the contaminated area. Two weeks after treatment, the EPG was 325 and 10 days later it was 25. Due to the unusual host, a molecular analysis of the parasite was performed, which confirmed the nematode as *H. contortus*. The authors note that monthly deworming, which was introduced more than 5 years ago, probably contributed to the development of multiple anthelmintic resistance in this *H. contortus* population. They concluded that proper use of anthelmintics and good pasture management are crucial to reduce the parasite burden in captive giraffes.

Lan et al. [62] described their experiences with the use of ivermectin in red pandas (*Ailurus fulgens*). Ten of the 48 animals died after suffering from prolonged depression, weight loss and xanthochromia of the mucous membranes. At post-mortem examination, live heartworms were found in the right ventricles and pulmonary arteries of all ten animals. Selamectin and ivermectin were used for clinical prophylaxis in the remaining red pandas, with a gradual decrease in morbidity and mortality observed. Thereafter, all red pandas received prophylactic treatment with ivermectin instead of selamectin at monthly intervals, as ivermectin was more suitable for long-term prophylaxis without the need to anesthetize the animals prior to oral administration. However, regular fecal examinations showed that the pandas were infected with *Baylisascaris ailuri* roundworms. The dose of ivermectin used as a preventive drug against heartworms was 6 µg/kg. In this case, the dose of 200 µg/kg was used to prevent both heartworms and *B. ailuri*. No case of dirofilariasis was observed that year. However, in the next year, four cases occurred in newborn pandas. Therefore, heartworm chemoprophylaxis was administered to all red pandas, including cubs, and no more cases of *Dirofilaria immitis* were observed. The authors recommend lowering the preventive dose of ivermectin against heartworms in pandas to 50 µg/kg and treating young pandas as soon as possible after birth and then ongoing treatment with a monthly dose.

Since we did not find any results on the deworming of captive Macropodidae, and given that they are common zoo inhabitants, we decided to include the study by Cripps et al. [63] in the present review. Field trials were conducted to treat free-living eastern grey kangaroos (*Macropus giganteus*) with the anthelmintics moxidectin, ivermectin and albendazole. The anthelmintics were administered according to the doses recommended for domestic animals by the individual anthelmintic manufacturers: moxidectin (Cydectin® long-acting injection for cattle, 1 mg/kg subcutaneous, Fort Dodge, Baulkham Hills, NSW, Australia)—as a single dose (1 mg/kg, SC) and as a double dose (2 mg/kg, SC).); ivermectin (Ivomec® injection for cattle, Merial, Parramatta, NSW, Australia)—single dose (200 mg/kg, SC); albendazole (oral Alben® for sheep, lambs and goats, Virbac Animal Health Pty. Ltd., Sydney, Australia)—3.8 mg/kg, PO. Unexpectedly, moxidectin and ivermectin had low efficacy with maximum FEC reductions of 2% and 28%, respectively. However, treatment with albendazole reduced FEC in all kangaroos by 100% and despite the short duration of action of albendazole, FEC remained low for up to 3 months. Macrocyclic lactones at the recommended dose were far less effective against strongylid nematodes in kangaroos than in domestic herbivores. According to the authors, this may be due in part to the pharmacokinetics in the host and in part to the low susceptibility of some of the nematodes that infest eastern grey kangaroos. Cripps et al. [63] concluded that macrocyclic lactones at the doses tested were of little benefit for the treatment of kangaroos with parasite infections. Instead, they considered oral doses of albendazole to be potentially useful, but only if the animals can be trapped and treated at intervals of (at least) 3 months. According to Cripps et al. [63], the length of time between albendazole treatments in macropodids needs to be investigated to determine safe repeat intervals.

Laconic data on rhinoceros deworming has been found. In a review article on the medical problems of rhinoceroses in captivity and in the wild, Silberman and Fulton [64] pointed out that some anthelmintics that have been successfully used to treat intestinal nematode infestations in black and white rhinoceroses are dichlorvos (36.5 mg/kg body weight) given once, and mebendazole (15–20 mg/kg body weight) given once daily for 3 treatments.

3.8. Other Studies

Isaza et al. [65] used a mailed questionnaire survey to document the methods of parasite control currently used in captive wild ruminants. The majority of respondents indicated that they used similar parasite monitoring and identification techniques to those used in domestic ruminants. Of the four main anthelmintic classes, benzimidazoles and ivermectin were the most used. Many of the parasite control programs had a high treatment frequency, similar to the dosing frequency that has reportedly led to anthelmintic resistance in domestic animals. The lack of efficacy of benzimidazoles was perceived as a problem by many respondents.

An in vitro thiabendazole egg hatch test was used to detect BR in 7 antelope collections [66]. The aim of the study was to measure the prevalence of BR and to determine whether the occurrence of BR was related to the frequency of anthelmintic use. The frequency of prophylactic deworming per year was as follows: twice in one of the collections, four times in three of the collections, 6 times in one and 12 times, i.e., monthly, in two of the collections. Fenbendazole and ivermectin were used for treatment in all cases. In addition, pyrantel was used in one collection, morantel in one, albendazole in one and levamisole, oxibendazole and pyrantel in two collections. Six of the seven collections showed signs of BR. Only in the collection with prophylactic deworming twice a year was no resistance detected. The study shows that BR is widespread in antelopes in Florida and that the parasite control methods used in these collections, especially the high frequency of treatment, are positively correlated with the development of BR.

The efficacy of Zanide L forte® (Spectra Vet, Amman, Jordan, levamisole-0.75 g and oxyclozanide-1.00 g) on the gastrointestinal nematodes of ungulates and anthelmintic resistance status in a zoo in Nepal was evaluated by Kiju et al. [67]. The efficacy of the drug was 85% on day 7 and 89% on day 14 using hierarchical modelling of FEC and 86% on day 7 and 90% on day 14 according to the World Association for the Advancement of Veterinary Parasitology guidelines. According to the authors, this study represents the first documented case of ineffectiveness of anthelmintic treatment leading to anthelmintic resistance in the Central Zoo of Nepal, which requires an appropriate and effective anthelmintic program. As part of broader preventive measures against the various parasitic infections in the mammals in the same zoo, Dhakal et al. [68] recommended deworming every 4 months. They also recommended diagnosing the parasites at the molecular level to determine the likelihood of cross-transmission of parasites between different mammalian orders and their zoonotic potential and monitoring the immunological status of suspected animals to assess their immunity in relation to the parasite load.

A recent study systematized the knowledge on the use of helminthophagous fungi against parasites infesting wild animals in captivity [9]. It described the types of fungi, their forms, the animal species to which they were administered and the resulting reduction in viability of certain parasite species. The study cited impressive data, for example, that the application of *D. flagrans*, *M. circinelloides* and *Trichoderma atrobrunnenum* reduced the viability of equine strongyle larvae, *Parascaris equorum* and *Trichuris* sp. parasites in zoo herbivores by 84–89%, 61–67% and 13–50%, respectively. Based on the data collected, Salmo et al. [9] concluded that saprophytic filamentous fungi can destroy or inhibit the development of certain parasites in feces and/or soil. This is of great importance for the control of various parasites infesting wild animals in zoological parks, where the administration of chemical parasiticides commonly used on livestock seems to be the only solution. To improve parasite control programs in zoos, the authors suggest that appropriate deworming of animals with anthelmintics should be carried out together with the safe method of periodical administration of chlamydospores from saprophytic soil fungi.

In the Dehiwala National Zoological Gardens in Sri Lanka, regular deworming of the animals was carried out every three months [13]. Nevertheless, a study in the zoo showed a high prevalence of gastrointestinal parasites in mammals. According to the authors of the study, their findings underline the importance of fecal analysis prior to the administration of deworming and the use of a more targeted approach to control pathogenic species.

4. Discussion

4.1. Anthelmintics Used

The overview data show that the control of helminthoses is currently mainly based on the use of anthelmintics. Captive herbivorous mammals have been treated with anthelmintics with three main objectives—cure of clinically manifested cases, prophylaxis and investigation of the pharmacological properties and efficacy of the drugs. Anthelmintics from the benzimidazole group were used most frequently (Table 1). Fenbendazole was used in blackbuck, Arabian oryx, scimitar-horned oryx, slender-horned gazelles, Soay sheep, Alpine ibex, red deer, Nelson's elks, antelopes, gazelles, giraffids, Indian elephants, impalas, dromedary camels, European bison, spotted deer, sambar, barking deer, giraffes, addax, Cuvier's gazelles, Thomson's gazelles and Grant's zebras [16,25,27,30,35,44,47,49,53,54,59]. Albendazole was used in elks, mouflons, deer, goats, blackbucks, elephants, Eastern grey kangaroos, spotted deer, and European bison [22,30,33,41,44,63,69]. Mebendazole was used in black and white rhinoceros, gazelles, and Indian elephants [18,20,44,64]. There was one report each on the use of cambendazole, oxfendazole and triclabendazole in black-tailed deer, blackbuck and Indian elephants [16,31,44]. Ivermectin was the most commonly administered macrocyclic lactone in zoo herbivores (Table 2). It has been used in antelopes, Bactrian camels, deer, ponies, mouflons, llamas, Soay sheep, ibex, elks, elephants, zebras, red pandas, kangaroos, Przewalski's horses and European bison [5,16,18,19,23,30,33,35–37,42,43,48,55,62,63,70,71]. The other class of anthelmintics used in captive herbivores are the imidazothiazoles (Table 3). Levamisole has been used in black-tailed deer, mountain reindeer, Arabian sand gazelles, Arabian mountain gazelles, Indian elephants and European bison [23,30,31,44,71]. There have been sporadic reports of the use of other anthelmintics such as dichlorvos, hexachlorophene, oxyclozanide, niclosamide, morantel tartrate and moxidectin [44,47,63,64] and several reports of the combined use of drugs [57,61,67].

Table 1. Systematized data on treatment with benzamidazoles in captive herbivorous mammals.

Medicine—Dosages and Schemes of Treatment	Animals	Parasites	Results and Conclusions	Source
Albendazole in a dosage of 15 mg/kg body weight mixed into the feed for 3 days.	Blackbucks	Strongylids	The reduction in FEC was 100% on day 3 after treatment and no recurrence of infection was reported until day 55 after treatment. Thus, albendazole proved to be 100% effective.	[22]
Albendazole 10 mg/kg for 5 consecutive days.	European bison	Gastrointestinal nematodes	The results of the FECRT ranged from 37.2 to 99.6%—unsatisfactory.	[30]
Albendazole 5 mg/kg	Spotted deer	Helminths	100% susceptibility to albendazole	[33]
Albendazole at a dose of 5 or 7.5 mg/kg in food, for high-risk groups.	Elks, Mouflons, Deer, Goats	Gastrointestinal nematodes	Readily accepted even by fastidious animals and when given at high peak periods, resulted in drops of infection.	[69]
Albendazole 5 mg/kg	Elephants	Strongylids	The animals recovered completely on the 7th day. EPG decreased from 700 and 671.4 to 78.57 and 50.	[41]
Albendazole 3.8 mg/kg	Eastern grey kangaroos	Strongylids	Reduced FEC by 100% for up to 3 months.	[63]

Table 1. *Cont.*

Medicine—Dosages and Schemes of Treatment	Animals	Parasites	Results and Conclusions	Source
Cambendazole 40–50 mg/kg as a drench.	Black-tailed deer	*Dictyocaulus viviparus*	Lungworm larvae were not recovered in feces 6 days post treatment, but were recovered again between 15 and 23 days post treatment.	[31]
Febantel—single dose of 3 mg/kg	Asian elephants	Helminths	FECR was 67.82% and 49.32% on day 7 and 28 after treatment respectively.	[46]
Fenbendazole 7.5 mg/kg—routine deworming (twice a year—in spring and fall)	Blackbuck	*Camelostrongylus mentulatus*, *Nematodirus spathiger*	Infections persisted.	[16]
Fenbendazole—milled into pellet feed and given to the animals over a period of 4 days instead of the regular pellet feed in fall, winter and spring.	Exotic ungulates	Nematodes	Posttreatment EPG was significantly lower ($p < 0.0001$) than pretreatment EPG for all target species and all enclosures.	[17]
Fenbendazole (Vetfen 600 pelleted feed having fenbendazole @ 600 mg/100 gm feed, Indian Immunologicals) at 100 g for 3 days.	Ladakhi goat	Strongylids *Trichuris* spp.	The reduction in FEC was 100% on day 3 and day 5 after treatment for strongylids and *Trichuris* spp. respectively. No eggs were detected up to 30 days after treatment.	[22]
Fenbendazole (Vetfen 600 pelleted feed having @ 600 mg/100 gm feed, Indian Immunologicals) at 150 g for 3 days in the feed.	Chinkaras	Strongylids *Trichuris* spp.	The reduction in FEC was 100% on day 3 and day 5 after treatment for strongylids and *Trichuris* spp. respectively. No eggs were detected up to 30 days after treatment.	[22]
Fenbendazole 7.5 mg/kg for 3 days	Impala	Helminths	Efficacy of 90%.	[25]
Fenbendazole at a dose of 3.3 g per animal, twice daily, for five consecutive days.	European bison	Gastrointestinal nematodes	The excretion of strongylid eggs from the subfamily Ostertagiinae was reduced from 81 to 30%. FECR—87% for *H. contortus*. Effective against *Nematodirus* and *Trichuris*.	[27]
Fenbendazole 10 mg/kg for 5 consecutive days.	European bison	Gastrointestinal nematodes	Values of FECRT > 95%.	[30]
Fenbendazole 7.5 mg/kg	Spotted deer, Sambar, Barking deer	Gastrointestinal nematodes	96.15% effective on the 14th day after treatment.	[35]
Fenbendazole—in the feed at a dose of 7.5 mg/kg body weight for three consecutive days. Fenbendazole has been administered over two years in spring, summer and fall.	Arabian oryx, Scimitar-horned oryx, Slender-horned gazelles, Soay sheep, Alpine ibex, Red deer, Nelson's elk	Gastrointestinal nematodes	Highly effective (reducing the excretion of nematode eggs by more than 90%) by scimitar-horned oryx, slender-horned gazelles, Soay sheep, red deer and Nelson's elk. Lower efficacy (<90%) was observed in Arabian oryx and ibex.	[53]
Fenbendazole oral suspension, 7.5 mg/kg, once daily, 3 days in succession.	Giraffe, Addax, Cuvier's gazelle, Thomson's gazelle	Gastrointestinal nematodes	66.66% drug efficacy.	[59]
Fenbendazole oral suspension, 10 mg/kg, once daily, 3 days in succession.	Grant's zebras	Gastrointestinal nematodes	66.66% drug efficacy.	[59]
Fenbendazole—repeated twice at 3-week intervals. A high initial dose (20 mg/kg) was followed by administration of the recommended dose (10 mg/kg).	Dromedary camels	*Trichuris* spp.	Two young male dromedary camels gradually recovered.	[49]
Fenbendazole—single oral treatment of 5 mg/kg or 2 doses of 50 g.	Indian elephants	*Murshidia* sp.	Effective.	[44]
Fenbendazole—12 g in 200 mL water in 2 divided doses 3 days apart.	Indian elephants	Trichostrongylids	Effective.	[44]
Fenbendazole 5 mg/kg	Indian elephants	Strongylids, Amphistomes	Effective.	[44]
Fenbendazole (Fentas 3 g bolus®) × 4, repeated after 15 days.	Indian elephant	Strongylids, *Strongyloides* sp.	No helminth eggs after 20 days of treatment.	[47]
Mebendazole—in three doses, depending on the species: *Gazella dorcas*, 14 mg/kg; *G. cuvieri*, 6 mg/kg; and *G. dama*, 3 mg/kg, PO, twice daily, for three consecutive days.	Gazelles	Gastrointestinal nematodes	FECs before/after treatment: 230/125—*G.dama* 292/618—*G. cuvieri* 107/480—*G. dorcas*	[18]

Table 1. *Cont.*

Medicine—Dosages and Schemes of Treatment	Animals	Parasites	Results and Conclusions	Source
Mebendazole 15–20 mg/kg	Cuvier's gazelle	Gastrointestinal nematodes	Poor results by all routes tested, including administration by drenching according to the manufacturer's recommendations. Reduction of shedding eggs between 47% and 67%.	[20]
Mebendazole 3–4 mg/kg	Indian elephants	Strongylids	100% effective.	[44]
Mebendazole 15–20 mg/kg, once a day, for 3 treatments.	Black and white rhinoceros	Gastrointestinal nematodes	It was successfully used.	[64]
Oxfendazole 4.5 mg/kg in supplementary feed, for 3 consecutive days, monthly.	Blackbuck	*C. mentulatus*, *N. spathiger*	Successfully reduced FEC and pasture larvae of *C. mentulatus*, but number of *N. spathiger* larvae on pasture was not affected.	[16]
Triclabendazole—9 mg/kg (up to a maximum of 7200 mg/animal).	Indian elephants	*Fasciola* sp.	100% effective.	[44]

Table 2. Systematized data on treatment with ivermectin in captive herbivorous mammals.

Dosages and Schemes of Treatment	Animals	Parasites	Results and Conclusions	Source
200 µg/kg IM by blowpipe	Blackbuck	*Camelostrongylus mentulatus*, *Nematodirus spathiger*	The infections persisted. Control was only achieved when various anthelmintics were administered monthly.	[16]
200 µg/kg SC	Gazelles	*Trichuris, Ostertagia, Cooperia, Trichostrongylus, Nematodirus, Strongyloides*	FECs before/after treatment: 132/13—*G.dama* 556/22—*G. cuvieri* 163/0—*G. dorcas*	[18]
200 µg/kg SC	Gazelles	*Nematodirus spathiger*	Reduction in average FECs between 94–97.2%.	[23]
Ivomec® SC or Eqvalan® IM 200 µg/kg (1 mL/50 kg and 1 mL/100 kg respectively)	Antelopes	*Nematodirus, Trichuris, Trichostrongylus, Ostertagia, Cooperia, Haemonchus, Chabertia*	The infection was cured, but the nematode eggs reappeared in the feces after 6 months and a second dose of 0.7–1.0 mL/animal resulted in a complete cure. No side effects.	[70]
600 µg/kg IM	Sable antelope	*Parelaphostrongylus tenuis*	Initial mild improvement, but eventually all animals either died or were euthanized due to complications of the disease.	[71]
200, 600, 1000 µg/kg SC	Mouflons	*Muellerius capillaris*, *Nematodirus* spp., *Oesophagostomum* spp.	A dose of 600 µg/kg body weight was recommended as optimal for the parenteral treatment of mouflon nematodes.	[19]
300 µg/kg PO	European bison	Gastrointestinal nematodes	Deworming proved to be ineffective against strongylids and *Trichuris* sp. FECRT ranged from 63.2% to 97.5%.	[30]
200 µg/kg PO for three days, administered three times at 5-week intervals	Antelopes, Soay sheep, Ibex, Deer, Elks	Variety of parasites	The early season ivermectin program resulted in very low to no egg shedding in gazelles, adult Soay sheep, ibex, red deer and Nelson's elk throughout the grazing season, but could not prevent high egg shedding in October in Arabian oryx and scimitar-horned oryx.	[55]
200 µg/kg PO	Spotted deer	Helminths	An efficacy of 97% was found, indicating low resistance status.	[33]
200 µg/kg PO	Spotted deer, Sambar, Barking deer	Gastrointestinal nematodes	FECRT has shown an efficacy of 97%.	[35]
100 µg/kg PO	Przewalski's horses	Large and small strongyles	The fecal egg count reduction was almost 100%.	[5]

Table 2. *Cont.*

Dosages and Schemes of Treatment	Animals	Parasites	Results and Conclusions	Source
Eqvalan® 200 µg/kg IM	Shetland ponies	Strongyles, *Parascaris equorum*	Infection-free for three months with fortnightly fecal examinations. No side effects.	[70]
400 µg/kg PO	Ponies	*Cyathostoma* sp., *Oxyuris equi*	It was highly effective in the infection with cyathostomes. *O. equi* was resistant.	[37]
Medicated feed pellets (with 10 mg ivermectin per kg)	Zebras	Intestinal strongyles	The drug showed an efficacy of 100% for up to 78 days after treatment.	[36]
200–400 µg/kg PO	Elephants	Variety of parasites	Suitable to eliminate many types of parasites in elephants and could minimize the development of parasite resistance.	[42]
10 mg/100 kg SC	Elephants	Microfilariae	Effective for the elimination of microfilariae for up to 3 months. Also significantly reduces the number of gastrointestinal nematodes.	[43]
Ivomec® SC at 200 µg/kg (1 mL/50 kg)	Bactrian camel	*Trichuris*	The treatment was ineffective against severe infections. No side effects.	[70]
200 µg/kg single SC injection	Llamas		Ivermectin levels—undetectable in plasma collected up to 4 weeks after injection, suggesting that the dosage used is insufficient to achieve therapeutic concentrations in this species.	[48]
200 µg/kg	Red pandas	*Dirofilaria immitis*, *Baylisascaris ailuri*	No side effects. The authors advised reducing the preventive dose of ivermectin against heartworms to 50 µg/kg, which is known to be well tolerated by gravid or young animals.	[62]
200 µg/kg SC	Kangaroos	Strongyles	It was much less effective against strongylid nematodes in kangaroos than in domestic herbivores: maximum FEC reductions of 28%.	[63]

Table 3. Systematized data on treatment with levamisole in captive herbivorous mammals.

Dosages and Schemes of Treatment	Animals	Parasites	Results and Conclusions	Source
7.5 mg/kg	Reem gazelles, Idmi gazelles	*Nematodirus spathiger*	Reduction of the average FECs in the Reem gazelles—89.3%, in the Idmi gazelles—96.4%.	[23]
7.5 mg/kg PO	European bison	Gastrointestinal nematodes	Levamisole was used at one location; in this case the egg count was below 100 EPG and the samples were excluded from the ECRT analysis.	[30]
16 mg/kg as a drench	Black-tailed deer	*Dictyocaulus viviparus*	A temporary decrease in the production of larvae.	[31]
5.5–11 mg/kg SC	Reindeer	*Parelaphostrongylus tenuis*	Initially mild improvement, but eventually all animals died.	[71]
3 mg/kg	Indian elephants	Strongylids	100% effective	[44]

Properties such as broad-spectrum anthelmintic activity, ovicidal activity, a particularly wide safety margin and ease of oral administration [72] have most likely led to the choice and frequent use of the benzimidazoles. Ivermectin also has a wide margin of safety in herbivores [73]. This and its other advantages such as its broad spectrum of antiparasitic activity (not only against internal but also against external parasites), the possibility of parenteral administration, its long-term existence in the body and the lack of induction of cross-resistance to other commonly used antiparasitic agents [74] have made it the second choice for use in captive herbivores. The present study showed that the doses of benzimidazoles and ivermectin administered to captive herbivores were in most cases close to the doses recommended for livestock and horses [75], and when higher doses were used, no side effects were observed. Although we found no data on side effects following administration of levamisole to captive herbivores, it should be used with caution as it has a low safety margin and cases of poisoning have been observed following overdose in livestock [76,77]. The following should be noted about other preparations for which data was found: Dichlorvos and hexachlorophene are not only outdated but also highly toxic and have been for a long time replaced by more effective and less toxic agents. Morantel is not effective against mucosal or arrested stages of nematodes or against lungworm infections. The salicylanilides oxyclozanide and niclosamide are normally marketed as flukicides for livestock and could be adapted as needed for captive herbivores. Moxidectin is effective against a wide range of nematodes and arthropods and would be a suitable alternative for use where other macrocyclic lactones are less effective.

4.2. Treatment Results and Ways to Improve Them

The success of the treatment was not always completely clear. In most cases, a relatively high efficacy of the drugs was reported, but this was mainly observed in the first period after treatment (10–14 days), with indicators soon changing [12,26]. In other cases, only a temporary decrease in parasite egg and larvae production and a slight improvement in animal condition were observed [31,61,71]. The results of treatment with the same drug varied depending on the animal and parasite species [16,23,27,37,53,55] and cases of poor outcomes following anthelmintic treatments or persistence of parasitoses have been documented [16,20,30,63,67].

The development of resistance of helminth populations to administered drugs has been discussed as one of the main reasons for ineffectiveness of anthelmintic treatment. Frequent use and underdosing of anthelmintics were the most important prerequisites for this [5,29,61,65,66], but Kuzmina et al. [39] consider underdosing to be the more important factor of the two.

Underdosing often occurs in zoo herbivores because the most used oral anthelmintics are not always readily accepted by the animals. Anthelmintics have been incorporated into salt licks [25] or medicated feed in the form of pellets to avoid the stress of forced administration and to facilitate routine use [17,36,53]. However, medicated feed should also be used with caution, especially in species that have a strict feeding hierarchy, such as zebras, where dominant animals may ingest more than others [36]. Experience has shown that individualized treatment through use of anthelmintic formulations that are less prone to underdosing, e.g., pour-on solutions, is preferable [60], and that the route of drug administration is more important in the treatment of certain helminth species than others [21]. Ortiz et al. [21] compared seven different methods of administering ivermectin to gazelles and found that for parasite problems caused by *Nematodirus* species, in contrast to other strongylids, direct administration to individual animals is preferable.

4.3. Factors That Influence Control

Limited housing space, high contamination of grass with infective eggs/larvae and difficulties in cleaning and dung removal are among the main problems in the successful control of helminthoses in captive herbivores [15,16,25,26,32,55,56]. For example, one study has shown that strongylids persist in zebra and camel enclosures, where a thousand eggs and larvae were found in 1 kg of soil and grass [78]. These factors favor the accumulation of invasive parasite stages, and this is a prerequisite for reinfection after successful treatment. It has also been purported that irregular dung removal is beneficial. For example, Tang et al. [5] report that a low treatment frequency and inadequate dung management slow down the development of anthelmintic resistance because there are a large number of eggs and free-living larvae of susceptible genotypes in the pasture, also known as the refugia population. Tang et al. [5] believe that increasing the refugia population could even restore anthelmintic efficacy. Clearly, it is a question of balance between the various factors in management under the specific conditions of husbandry.

4.4. Prophylactic Deworming

There is no clear answer to the question of whether, when and how often prophylactic deworming of captive herbivorous mammals should be carried out. A frequency of 2 times/year is common [26,32,66]. According to Isaza et al. [66], this frequency was optimal to avoid the development of anthelmintic resistance. However, the environmental conditions that favor the year-round presence of infective larvae on pasture make parasite control difficult and may require frequent anthelmintic treatments (>3/year) for adequate results [17]. Under such conditions, even deworming four times a year was not satisfactory [13]. On the other hand, the study by Isaza et al. [66] showed that a high frequency of deworming (4, 6 and 12 times per year) was positively correlated with the development of BR. The multidirectional effect of prophylactic deworming emphasizes the need to develop long-term strategies to control helminthoses in captive herbivores based on the specific conditions in zoos and accompanying parasitological examinations. Identification of species that are highly infected and knowledge of the seasonal variation of their helminths can contribute significantly to a well-coordinated species-specific management and helminth control program [54]. For example, in the study by Goossens et al. [54] at Antwerp Zoo, no routine anthelmintic treatment was carried out because no helminthosis was suspected in the previous 5 years. The same group of authors [32] point out that nematode infections are of minor importance when keeping animals in dry enclosures with sandy soil and that anthelmintic treatment in herds consisting of adult, non-reproductive animals appears unnecessary as long as the composition of the herd remains stable. The frequency and dose of prophylactic treatments in zoo herbivores should be improved according to the taxonomic groups of host and parasite [60]. Practices have been introduced to monitor nematodes with concomitant quantitative ovodiagnostics and to initiate treatment when EPG exceeds a certain threshold, e.g., 400 in captive wild equid feces [34], 150 in zebra feces [39], and 200 in camelids [52]. However, EPG values should be lower in the case of infection with *Trichuris, Capillaria* and *Nematodirus* [52]. The overview reflects some peculiarities related to host taxonomy that should be taken into account, such as: Goats and elk require higher doses of fenbendazole than sheep and red deer because they metabolize the drug more rapidly [53]; reindeer develop age-related immunity to *Trichuris* spp., whereas elks fail to do this [32]; zebras rarely eat food containing anthelmintics, so it is very likely that they receive a lower dose of the drugs [39]; *Haemonchus* is known to cause severe anemia and protein loss without significant weight and condition loss in moderate to severe infection, but in most cases camelids do not show weakness from anemia until their blood levels are very low, so they may die overnight if infested with *Haemonchus* and still look "normal" the day before [52].

4.5. Selection of Anthelmintic Agents

The choice of anthelmintics is very important for the success of deworming, especially if there is a greater likelihood of resistance developing to these drugs. According to Dr. Walker [52], it is best to use the oldest class of drugs, which still results in a 90% reduction in parasite eggs found in a fecal floatation. Isaza et al. [66] are of the opinion that in cases where BR is suspected, treatment trials measuring the efficacy of an anthelmintic in a group of animals should be conducted and that in collections where resistance is proven, the use of benzimidazoles should be avoided. As an alternative to benzimidazoles, they mention the avermectins (ivermectin), the imidothiazoles (levamisole), the tetrahydropyrimidines (pyrantel and morantel) and the organophosphates. The use of drugs from different classes in combination is recommended to increase efficacy and enable successful elimination of anthelmintic-resistant infections [61]. In general, methods of parasite control that require less use of anthelmintics should be sought [66]. Some studies have been conducted in this direction; copper oxide wire particles in bolus form have been promising as an anthelmintic alternative for exotic artiodactylids [24] and the addition of nematophagous fungi to feed has been successfully tested and recommended as a novel and useful contribution to the sustainable management of digestive parasite infections in captive herbivores [9,26,34,38,79].

5. Conclusions

The review data show that the control of helminths in captive herbivores is currently mainly based on the use of anthelmintics, with benzimidazoles and ivermectin being the most commonly administered. The anthelmintics were administered at doses similar to those used in farm animals and sometimes at higher doses, with no evidence of side effects. Treatment results often depended on the animal and parasite species. Incomplete cure, reinfection and resistance to anthelmintics were the most common problems in the field. Preventive medicine should be the basis for the control of helminths in captive herbivores. The necessity, frequency and timing of preventive deworming should be assessed individually for different facilities. The optimal prevention measures include the following: quarantine of newly arrived animals; daily or as intensive as possible cleaning of droppings; regular change of substrate in the enclosures; and monitoring of possible infections and their qualitative and quantitative composition (monthly or at least every two months). For treatments and monitoring effectiveness, recommendations include the following: individual assessment of the need for treatment; selective choice of anthelmintics; post-treatment examination between the 10th and 14th day after deworming; carrying out group treatment after a preliminary drug effect test; and conducting mass deworming only in case of where there is significant increase in fecal egg counts, highly pathogenic helminth species and a deterioration in the condition of the animals. In the future, more attention should be paid to new approaches, such as biological control by saprophytic fungi or natural compounds as an alternative to anthelmintics. This would help to minimize the use of anthelmintics, protect refugia and allow animals to remain healthy by maintaining a balance with the low levels of parasites present.

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