

Review on Anthelmintic Resistance of Nematodes of Small Ruminants in Ethiopia

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Abstract: The development of anthelmintic resistance poses a large threat to the production and welfare of grazing animals globally. Development of variable degrees of resistance among different species of gastrointestinal nematodes has been reported for all the major groups of anthelmintic drugs. The degree and extent of this problem especially with respect to multidrug resistance in nematode populations is seriously increasing problem at alarming rate in different parts of the world including Ethiopia. In Ethiopia, various anthelmintic have been used in different parts of the country for the treatment of sheep and goats helminth parasites. The three most important genera, *Haemonchus*, *Teladorsagia* and *Trichostrongylus* are among the multiple anthelmintic resistant populations of parasites in small ruminant. The factors considered most significant for the development of anthelmintic resistance include excessive frequency of treatments, prophylactic mass treatment of animals and under dosing. Maintaining parasites in refugia and not exposed to anthelmintics, seems to be a key point in controlling and delaying the development of resistance. Targeted selective treatments attract the interest of scientists towards this direction. Additionally, adoption of strict quarantine measures and a combination drug strategy are two important methods of preventing of anthelmintic resistance. Experience from the development of anthelmintic resistance suggests that modern control schemes should not rely on sole use of anthelmintics, but employ other, more complex and sustainable recipes, including parasite resistant breeds, nutrition, pasture management, nematode-trapping fungi, antiparasitic vaccines and botanical dewormers. In this way, anthelmintic resistance may be delayed and the effectiveness of anthelmintic drugs may be prolonged. Therefore, directing research toward the antiparasitic vaccines and botanical dewormers should be encouraged as alternative to the use of anthelmintics.

Key words: Anthelmintic • Nematode • Resistance • Refugia • Small Ruminant

INTRODUCTION

The use of modern broad spectrum anthelmintics, since their introduction in the 1960s, has been a convenient and often efficient method to control parasite infections in grazing livestock. However, failure to adequately control infections because of the development of anthelmintic resistance in worm populations [1, 2] and extensive use of anthelmintics has led to the world-wide spread of Anthelmintic resistance in the animal industry [3]. Resistance to available veterinary anthelmintic drugs was reported soon after their introduction. Resistance among sheep nematodes to Thiabendazole (TBZ) and

Ivermectin (IVM) was reported in 1964 and 1988 among both laboratory-selected and field strains of *Haemonchus contortus* in South African sheep respectively [4].

The importance of resistance to the three groups of broad spectrum anthelmintics (The benzimidazoles (BZ), imidazothiazoles (levamisole, LEV) and hydroxyprymidines (pyrantel/morantel) and the macrocyclic lactones (avermectins and milbemycins, ML) have increased dramatically in nematodes of sheep and goats in many parts of the world [5]. Since the publication of the World Association for the Advancement of Veterinary Parasitology (WAAVP) methods for the detection of anthelmintic resistance in 1992, Coles, *et al.* [6]. work in

South Africa [7], Australia [8] and the UK [9] stress that resistance is present to all three broad-spectrum anthelmintic groups and therefore, production is threatened.

In Ethiopia, various anthelmintics have been used in different parts of the country for the treatment of Sheep and Goats helminth parasites [10, 11]. Some researcher reported existence [12] and some others absence of anthelmintic resistance [10, 13] in the region. Albendazole was suspected for development of resistance, while Ivermectin and Tetramisole were found to be effective [14].

According to Getachew, *et al.* [15] no anthelmintic resistance of Albendazole, Tetramisole and Ivermectin found to be detected from clinical cure point of view but the population of *Haemonchus contortus* that has escaped the treatments deserves further scrutiny as this parasite is the most prolific and highly pathogenic in sheep. This cannot generalize that there is no anthelmintics resistance because the absence of resistance could also be explained by the low sensitivity of the fecal egg count reduction test which detect levels of resistance below 25% [16].

Understanding the development of Anthelmintic resistance and diagnose by sensitive detection technique *in vivo* or *in vitro* at an early stage and the spread of resistance alleles in parasitic helminths is crucial to prolonging the efficacy of current anthelmintics. It will also be beneficial in the design of new chemotherapeutic agents to overcome or prevent resistance and the identification of new drug targets. Despite notable ongoing activities to identify and evolve new anthelmintic classes by a shrinking list of institutions, there is doubt that we will see the release of a product with a new mode of action in the livestock area in the near future [4].

Use of only and similar anthelmintics drugs coupled with indiscriminate use increases the risk of development of resistant parasite populations at alarming rate. Despite the fact that Different diagnostic assays for the detection of anthelmintic resistance are available current trends of using conventional anthelmintic resistance detection tests suffer from lack of sensitivity to early diagnose anthelmintic resistance. This reduces numbers of nematodes in refugia [17] and will accelerate selection for resistance. If the continued spread of resistance is to be slowed, tests are required to permit the resistance status of farms to be determined to aid in planning the optimal use of the remaining effective anthelmintics.

Therefore, in light with the above background information, the objectives of this review include:

- To review the anthelmintic resistance in nematode parasites affecting small ruminants
- Overview factors affecting the development of anthelmintic resistance
- Provide possible control and prevention strategies for anthelmintics resistance

Anthelmintic Resistance: There is considerable debate about the definition of resistance and ‘tolerance’ is used to describe the stage between success and failure of drug treatment. However, as stated by Coles [18], resistance occurs when a susceptible population shows any decrease in response to treatment and is complete when the maximum dose of drug that can be tolerated by the host has no effect. According to the World Association for the Advancement of Veterinary Parasitology (WAAVP), anthelmintic resistance is defined as failure to reduce faecal nematode egg counts (FEC) by at least 95% [6] and this definition is generally accepted diagnostically. It is a heritable trait and a nonreversible condition [5].

In an attempt to provide a scientific basis for resistance, resistance has been identified by an increase in the proportion of organisms in a population carrying a gene demonstrated to be linked with resistance. These heritable changes can be either genetic (including mutations, deletions or amplifications of specific genes) or epigenetic (where by methylation of genes or promoter regions of the genes change the gene expression in response to the drug) [19].

Status of Anthelmintic Resistance in Small Ruminants in Ethiopia:

In Ethiopia, various anthelmintics have been used in different parts of the country for the treatment of sheep and goats helminth parasites [10, 11]. The use of anthelmintics has been practiced for a long time and constitutes a considerable share of the costs spent by the country in the control of helminthosis [11]. Also, smuggling and misuse of veterinary drugs involving anthelmintics is a wide spread practice in the country [20].

Some of these drugs, particularly albendazole and tetramisole, have been continuously imported and distributed to every corner of the country under different trade names and by different manufacturers [21]. There was a complaint by the Regional Animal Health Officers and some animal owners with regard to the effectiveness of available anthelmintic, especially albendazole [14].

Table 1: Summary of some of anthelmintic suspected for resistance in Ethiopia

Study area	Nematode parasites reported	Anthelmintics used	Anthelmintics suspected for resistance	Authors
Sidama Zone	Mixed GIT Parasite	Albendazole, Tetramisole, Ivermectin	Albendazole	Sheferaw, <i>et al.</i> [14]
Bedelle zone	<i>Haemonchus</i> spp in sheep	Albendazole, Tetramisole, Ivermectin	None	Getachew, <i>et al.</i> [15]
Woliata sodo		Albendazole, Tetramisole And ivermectin	None	Sheferaw, <i>et al.</i> [13]
Hawassa	<i>Haemonchus</i> in Goat <i>Teladorsagia</i> in Goats	Albendazole, Tetramisole and Ivermectin ALbendazole, Tetramisole and Ivermectin	Albendazole, Tetramisole and Ivermectin Ivermectin	Kumsa and Abebe [12]

Factors Affecting the Development of Anthelmintic Resistance: The development rate of anthelmintic resistance appears to be slow at first, but once a certain level of resistance genes has been established, the following treatments result in an exponential increase of these resistance genes to a level where treatment failure occurs. Anthelmintic resistance factors act either independently or in an additive fashion and may be associated with the parasite species, the infected host, drug treatment, on-farm control management or the environment. The more intensively parasites are controlled with drugs, the more likely resistance will develop. Once resistance is present in a parasite population, there is no evidence of reversion or loss of resistance [22]. The dynamics of the selection for anthelmintic resistance of parasites in sheep have been well studied [23] and some predisposing factors are likely to be similar in the nematode parasites of cattle [3].

Parasite Genetics and Biology: Due to their genetic diversity, parasites in a population do not respond uniformly to treatment. The high genetic diversity is linked to the huge population size and high reproduction rate of parasites [24]. It is presumed that resistance alleles already exist within the parasite population, prior to the first introduction of a drug [5]. However, an alternative hypothesis suggests multiple origins of resistance by spontaneous and recurrent mutations [25]. Moreover, resistance develops faster if the genes are dominant rather than recessive: both heterozygote and homozygote worms will survive the treatment and contribute to the next generation [26].

Parasites have biological characteristics that favor resistance alleles to build up faster in the population, such as their direct life cycles (no intermediate host), a short generation time and high fecundity. It is assumed that, if resistant parasites have enhanced fitness or if resistance is linked to other fitness genes, the spread of resistance in the population will also increase. Fitness includes all properties that enable more worms to complete their life cycles, such as the egg-laying rate, the persistence of worms in the host (a reduced hypobiosis shortens their life cycles), survival on the pasture, the ability to migrate on herbage and their infectivity when ingested [26].

Refugia and Management Factors: Refugium is the parasite population, which is not exposed to anthelmintic treatment. The larvae on pasture, the percentage of animals left untreated and the arrested larval stages not affected by treatment of the host determine the parasites in refugia. The proportion of parasites in refugia needs to be optimal in order to dilute out the resistant genes in the pool of susceptible genes. Hence, the development of anthelmintic resistance is delayed without causing clinical disease. The parasites in refugia, the frequency of anthelmintic treatment and the extent of under dosing are mainly responsible for inducing anthelmintic resistance [27].

To decrease the selection pressure, it is of major importance that treatment and pasture management are fulfilled in ways that maintain refugia. Anthelmintic treatments should progress according to a strategic plan, where frequency, time of treatment and the selective treatment of first-year or infected animals are tightly followed. Short interval treatments that approach the prepatent period for the parasite, reduce the opportunities for susceptible worms to reproduce and diminish the parasites in refugia. On farms with an intensive breeding and/or grazing program, calves are given multiple treatments and are grazed away from the adults. Hence, pasture contamination derives from worms surviving short interval treatments, which creates a selection pressure on anthelmintic resistance to develop [28]. Therefore, it is encouraged to implement an alternate grazing system, where calves are allowed to graze on pastures used by older animals the year before [26].

It should also be avoided to treat animals and immediately moving them to a clean pasture. By doing so, contamination of the new pasture will only be attributed to a subpopulation that is resistant to treatment. In this respect, farmers should be aware that summer drought is a variable factor that clears out the free-living stages on pasture [28]. Additionally, bought in animals should be effectively quarantine drenched before they are placed on pasture in order to dilute out the progeny of survivors of the quarantine treatment [29].

Sub Therapeutic Drug Levels: To ensure that treatments are fully effective, it is important to weigh the animals first,

so that the anthelmintic drug can be given at the correct therapeutic dose level. However, the use of an average weight to determine a dose for an entire flock might lead to under dosing and selection for resistance in the largest animals [30]. Several laboratory experiments have shown that under dosing contributes to the selection of resistant or tolerant strains [31]. Reduced bioavailability of the drug has been associated with the route of administration and the type of animal. Especially the inconsistent performance of topical (pour-on) applications has been questioned as a predisposing factor for resistance. Moreover, the enhanced drug metabolism of some types of animals or breeds may contribute to the selection for resistance [32].

The selection pressure on the development of anthelmintic resistance is also affected by the pharmacokinetics of the drug. With the use of persistent (long-acting) or slow release drugs, the drug concentrations tail off slowly towards the end of their elimination phase as a result of an extended half-life. This effect has the same influence as under dosing animals. Therefore, short-acting drugs are preferably used [3, 33].

Single-Drug Regimens: Frequent and continuous use of a single drug leads to the development of resistance. For example, a single drug, which is usually very effective in the first years, is continuously used until it no longer works [34]. In a survey of sheep farmers in Tennessee [35] found that one out of every two flocks was dosed with a single anthelmintic until it failed. Long-term use of levamisole in cattle also led to the development of resistance, although the annual treatment frequency was low and cattle helminths seemed to develop resistance less easily than do worms in small ruminants. Frequent use of ivermectin without alternation with other drugs has also been reported as the reason for the fast development of resistance in *H. contortus* in South Africa and New Zealand [7].

Mass Treatment: Prophylactic mass treatments of domestic animals have contributed to the widespread development of AR in helminth. Computer models indicate that the development of resistance is delayed when 20% of the flock is left untreated [27] but it needs confirmation through experimentation. This approach would ensure that the progeny of the worms surviving treatment will not consist only of resistant worms. Leaving a part of the group untreated; especially the members carrying the lowest worm burdens should not necessarily reduce the overall impact of the treatment. In worm control in

livestock, regular moving of the flocks to clean pastures after mass treatment and/or planning to administer treatment in the dry seasons is a common practice to reduce rapid reinfection. However, these actions result in the next helminth generation that consists almost completely of worms that survived therapy and, therefore, might contribute to the development of AR [36].

Control and Prevention of Anthelmintic Resistance:

Complete eradication of gastrointestinal parasites on the pasture is not feasible. Instead, a low level of parasitism must be tolerated to trigger a protective immune response in the host, which will protect the animals in the following grazing seasons [37]. Measures that can be taken to reduce the larval pasture contamination and hence the number of treatments include mowing, late turnout on pasture and reduced stocking density [38]. Serum pepsinogen levels can be determined at the end of the grazing season to evaluate the applied worm prevention, which can then be optimized for the next batch of first-grazing season calves, if necessary [39].

Delaying the Onset of Anthelmintic Resistance Refugia:

Recently, the importance of the worm population in refugia for slowing down the development rate of anthelmintic resistance has been the focus of attention. This population is believed to be susceptible and provides a reservoir in which resistant parasites may be diluted. As the relative size of the refugia increases, the rate of evolution toward resistance decreases. Most parasitologists now consider levels of refugia as the single most important factor contributing to selection for anthelmintic resistant parasites [27]. Higher proportions of refugia may be achieved through a targeted selective treatment (TST) approach, where anthelmintic drugs are for example only administered to heavily infected individuals in the herd [39, 40]. This strategy is based on the fact that the majority of the worms reside in the minority of the animals [41].

Today, most cattle farmers apply a TST strategy but only to administer additional treatments during summer to animals that show signs of clinical PGE. However, a preventive TST approach should preferably be pursued. Unfortunately, for cattle, there are no convenient diagnostics to identify the animals in the herd that should be treated. FECs can be determined two months after the turnout, or the weight gain per animal can be monitored, but both approaches are too labor-intensive to be widely used [42].

A Combination Drug Strategy: Another advice farmer could take into account to reduce the development rate of anthelmintic resistance, is avoiding the use of the same class of anthelmintic drugs every year. In this way, the efficacy will be maximized and the longevity of the compounds will be prolonged [43]. The use of combination products may maximize the breadth of spectrum, may overcome species specific resistance profiles (dose-limiting species) and may delay the development and spread of resistance when the resistance allele frequencies are still low. Recently, the WAAVP guidelines have requested the approval of anthelmintic combination products for the use in ruminant livestock and in horses [44].

Synergistic combinations have been described for both human and veterinary infections. Synergism between Albendazole and ivermectin or diethylcarbamazine and between Mebendazole and levamisole or pyrantel has been described for the treatment of soil-transmitted helminth [45]. For veterinary parasites, a combination of Mebendazole and levamisole has been shown to be synergistic against *H. contortus* in sheep [46], febantel and pyrantel against *Ancylostoma caninum* in dogs [47], *Heterakis spumosa* in mice and fenbendazole and pyrantel against *Toxocaracanis in vitro* [48]. For the nematodes of small ruminants, the use of combinations serves dual purposes: to maintain nematode control in the presence of anthelmintic resistance, sometimes involving more than one parasite species and/or more than one class of anthelmintic; and concurrently, to delay the development of AR to the component chemical classes in those species in which resistance is not yet evident [49].

Adoption of Strict Quarantine Measures: Effective management strategies to prevent development of anthelmintic resistance are worthless if producers purchase resistant worms residing in breeding stock. This practice is more important than ever, as in recent years several farms with high-quality breeding stock dispersed herds where *H. contortus* and *T. colubriformis* were resistant to benzimidazoles and moxidectin. There is no faster way to spread resistance than to bring gastrointestinal nematodes to a farm. The current recommendation is to quarantine (on dry lot where feces can be removed) every new addition, dose with triple-class anthelmintic therapy and perform fecal egg count reduction tests [50].

Feed should be withheld for 24 hours before treatment, then moxidectin, levamisole and albendazole should be administered consecutively (do not mix drugs

together) at the appropriate dose for sheep or goats. Fourteen days later, treated animals should be evaluated by fecal egg count and fecal flotation techniques. The fecal egg count should be zero and flotation should yield very few or no eggs. Furthermore, after receiving this treatment, animals should be placed on a contaminated pasture. Never should an animal be placed onto a clean pasture after a triple anthelmintic class treatment regimen is administered, because any surviving worms will be triple resistant and there will be no refugia on pasture to dilute the future transmission of any eggs that are shed [50].

Nematode-Trapping Fungi: The philosophy behind biological control is that by using one of the natural enemies of nematodes, it will be possible to reduce the infection level on pasture to a level at which the grazing animals avoid both clinical and subclinical effects due to parasitic nematodes. Research with nematode-trapping fungi has documented the potential as a biological control agent against the free-living stages under experimental and natural conditions. These fungi occur in the soil throughout the world where they feed on a variety of free-living soil nematodes. These fungi capture nematodes by producing sticky, sophisticated traps on their growing hyphae[51]. For example, *nematophagous microfungi*, such as *Duddingtonia flagrans*, could be given in an oral formulation. After passage through the bovine gastrointestinal tract, they reduce pasture contamination by preying on the pasture larvae [52].

The above-mentioned technology has been applied successfully under field conditions in all livestock species and is an environmentally safe biological approach for control of worms under sustainable, forage-based feeding systems [53]. Biological control of parasitic nematodes in sheep seems to hold promise for the future, but to be able to assist producers, the optimal delivery system needs to be refined and further developed [54].

Genetic Improvement: Resistance is most likely based on inheritance of genes that play a principal role in expression of host immunity. Several breeds of sheep around the globe are known to be relatively resistant to infection. Using such breeds exclusively or in crossbreeding programs would certainly lead to improved resistance to worm infection, but some level of production might be sacrificed. Although such a strategy may be acceptable to some, selection for resistant animals within a breed also is a viable option. Within a breed, animals become more resistant to infection with age as their

immune system becomes more competent to combat infection [55]. Resistance can be identified by criteria such as consistent low fecal egg count and high packed cell volume, which can be used as a selection tool in production schemes [30].

Some animals within such a population do not respond well and remain susceptible to disease; therefore, the majority of the worm population resides in a minority of the animal population. It would make sense to encourage culling practices where these minority “parasitized” animals were eliminated, thus retaining more-resistant stock. This approach has been used successfully in some areas of New Zealand and Australia, but it may take a long time (up to 8–10 years) to achieve satisfactory results [56].

Improvement of Nutrition: The strongest link between nutrition and parasitism has been illustrated between protein intake and resistance to gastrointestinal nematode infection. The most dramatic has been abolishment of the periparturient egg increase in lambing ewes by providing protein at 130% of requirements. Immunity is closely related to protein repletion. There is conflicting documentation that sheep will decrease feed intake when initially infected with gastrointestinal nematodes [57].

Supplementation with phosphorus has been shown to prevent worm establishment. Cobalt deficiency also has been associated with reduced immunity to gastrointestinal nematodes. Adequate copper values are necessary for development of immunity to gastrointestinal nematodes. A promising work suggested that treatment of lambs with copper oxide wires orally reduced *H. contortus* burdens. However, copper toxicosis would be a concern associated with this treatment. Surprisingly, the addition of molybdenum at a concentration of 6-10 mg/d decreased worm burdens in lambs [58].

Pasture Management: A safe pasture is one that has not had sheep or goats grazed on it for 6 months during cool/cold weather or 3 months during hot, dry weather. Weaning sheep and goats at 2 months of age and rotating them through pastures ahead of the adults will minimize the exposure of susceptible animals to large numbers of infective larvae. Pastures should be subdivided into smaller lots to allow longer periods before regrading. Pastures that have become heavily contaminated because of mismanagement can be tilled and reseeded. Stocking rate is an important consideration in parasite control as it affects exposure to infective larvae and contamination of the pasture [59].

It is impossible to make a general recommendation on stocking rate as this will vary according to type of pasture, time of the year, current weather conditions and type of animal being grazed. Thumb rules include 5-7 goats or five sheep being the equivalent of one cow and suggestions of 5-7 goats/acre. Goats prefer to browse brush and trees, whereas sheep prefer to graze near the ground. Pasture management must include monitoring the condition of the herbage to ensure that overgrazing does not occur and to maintain a productive pasture [59]. Rotational grazing is a practice in which animals are allowed to graze a pasture and are then removed from it for a period of time before returning. This practice may allow the level of pasture contamination to fall drastically so that animals can be periodically introduced to cleaner pastures, reducing the number of larvae they are exposed to year-round [60].

In the early spring or at the onset to the rainy season, reduced pasture contamination is the most important aspect of control. Strategic deworming to remove arrested or recently emerged larvae before they contaminate the pasture will reduce pasture contamination. Treatment 2 weeks after a rain that removes recently acquired worms before they can begin passing eggs also will decrease pasture contamination. When plants high in condensed tannins are grazed, there is evidence that the incoming larvae are adversely affected as well as providing bypass protein for the host. If animals are allowed to browse, their chances of acquiring larvae diminishes as the distance from the ground increases. Most infective larvae are found within two inches (50 mm) of the soil surface [61, 62].

Antiparasitic Vaccines: As a consequence of drug resistance, efforts have increased in recent years to develop functional vaccines. This has been made possible by newer technologies in gene discovery and antigen identification, characterization and production. The increasing drug resistance of gastrointestinal nematodes has renewed intense interest in developing vaccines for these important veterinary pathogens. The most promising vaccine for small ruminant worms is based on a “hidden gut” antigen and specifically targets *H. contortus*. This antigen is derived from the gut of the worm and, when administered to the animal, antibodies are produced. When the worm ingests blood during feeding, it also ingests these antibodies [63].

The antibodies then attack the target gut cells of the worm and disrupt the worm's ability to process the nutrients necessary to maintain proper growth and

maintenance, thus killing the worms. This vaccine has been tested successfully only in sheep under experimental conditions and has had limited success under field conditions. Reasons for this lack of success are unclear. The drawback to this vaccine is that the antigen is normally “hidden” from the host and a number of vaccinations may be required to maintain sufficiently high antibody titer to combat infection. This process may be quite expensive. In addition, massive numbers of whole worms are necessary to extract limited amounts of antigen; therefore, this will only be practical when the antigen can be mass produced artificially via recombinant technology to lower costs [64].

Vaccines for other worms that do not feed on blood have focused on using antigens found in worm secretory and excretory products. These antigens have contact with the host and should stimulate continuous antibody production. However, protection has been quite variable and marketing of such products has not been pursued. Additionally, immunologic control of worm infections through vaccination could be the answer to anthelmintic resistance. However, despite the identification of several candidate protective antigens, no vaccines against gastrointestinal nematode parasites are currently available [64].

Botanical Dewormers: In last two decades, there has been a resurgence of interest in traditional health-care practices all over the world. These traditional practices involve diagnostics, herd grazing and pasture management as well as manipulation and treatment. The incidence of AR has simply forced veterinarians/producers to adopt alternative control strategies. Plants have been used from ancient times to cure diseases of man and animals. A number of medicinal plants have been used to treat parasitic infections in man and animals. There are many plants which have been reported in the literature for their anthelmintic importance. Among the most common medicinal plants which have anthelmintic effect are *Allium sativum*, *Nigella sativa*, *Artemisia* spp., *Balanites aegyptiaca*, *Acacia* spp., cucurbit (pumpkin seeds), *Commiphora molmol* (Myrrh), *Calendula micrantha officinalis*, *Peganum harmala* and Tumeric (curcumina) [65].

Additionally, various pasture tanniferous plants have also been investigated for potential effect against either incoming parasite larvae and/or already established worms. It has been postulated that the beneficial effects of tanniferous plants against internal parasites could be due to one, or a combination, of the following factors.

Tanniferous plants increase the supply and absorption of digestible protein by animals. This is achieved by tannins forming non-biodegradable complexes with protein in the rumen, which dissociate at low pH in the abomasum to release more protein for metabolism in the small intestine of ruminants; in other words, “natures protected protein”. This indirectly improves host resistance and resilience to nematode parasite infections. These plants can be a promising future for the control of worms which had previously shown resistance to synthetic drugs [62].

CONCLUSION AND RECOMMENDATIONS

Anthelmintic resistance of nematode parasites in small ruminants is an increasing worldwide problem occurring as a consequence of a number of factors related to drug products and management factors. Most worm control strategies rely heavily on the use of anthelmintics. However, the use of similar anthelmintics drugs coupled with indiscriminate use increases the risk of development of resistant parasite populations. Development of anthelmintic resistance could be prevented by avoiding frequent dosing and under dosing, while strategic deworming seems to be an appropriate option to treat animals. Measures should be suggested to avoid or delay the development of anthelmintic resistance. Furthermore, it should be stressed that any adjustments of worm control programs are case specific, since they depend on the treatment history and the pasture management of the farm. Sustainable control strategies for helminthosis may require an integrated approach incorporating environmental management and require a combination drug strategy in order to minimize the pressure for parasite adaptation.

Based on the above conclusion the following areas of focus are recommended:

- Frequent and unnecessary treatments of anthelmintics should be avoided, opting instead for strategic deworming.
- Strict quarantine measures and a combination of drug strategy should be implemented
- Dosing of animals and strategic deworming should be practiced by both animal health workers and veterinarians.
- Experimental research should be directed toward the antiparasitic vaccines and botanical dewormers.
- Enforcing national drug use policy is one priority area in order to combat the growing resistance by controlling illegal circulation of drug in country.

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