International Journal of Chemical Studies

P-ISSN: 2349–8528
E-ISSN: 2321–4902
IJCS 2018; 6(2): 1755-1762

Received: 08-01-2018
Accepted: 10-02-2018

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An overview of anthelmintic resistance in gastrointestinal nematodes of livestock and its management: India perspectives

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Abstract
Gastrointestinal (GI) nematode infections are one of the most prevalent and important issue upsetting the livestock worldwide. The principal mode of control of GI nematodes is based on anthelmintics because it is simple, cheap and offers both therapeutic and prophylactic cover against GI helminths. But, due to the emergence of resistant against anthelmintics, the problem has become complicated. The problem of anthelmintic resistance in GI nematodes of ruminants is worldwide in distribution. It has been documented to all classes of anthelmintics and multi-class resistance exists in many domestic animals. The objective of this review article is to provide an overview on the prevalence of anthelmintic resistance in India, mechanism and the factors contributing towards anthelmintic resistance, detection methods and to outline some strategies that may be used in parasite control programmers.

Keywords: Gastrointestinal nematodes, Anthelmintic resistance, Prevalence, Mechanism, Detection methods, Management

1. Introduction
Gastrointestinal (GI) nematodes are of major economic importance in domesticated animals throughout the world. They are responsible for blood loss, depression of appetite, impaired GI functions, alterations in protein, energy and mineral metabolism, change in water balance, increased mortality, decreased live weight gain, wool growth / yield, fertility and milk production, rejection of carcasses or organs for human consumption and predisposing to other diseases [1]. The extensive use of anthelmintics for control of GI nematodes has resulted in the development of resistance to one or more of the widely used anthelmintics in many countries [2]. It has been observed that frequent usage of the same group of anthelmintic; use of anthelmintics in sub-optimal doses, prophylactic mass treatment of domestic animals and frequent and continuous use of a single drug have contributed to the widespread development of anthelmintic resistance in helminths. Today anthelmintic resistance is recognized as a problem worldwide involving the main anthelmintic families. The definition of resistance varies in different publications. The following definition is given in the Guideline on anthelmintic combination products targeting nematode infections of ruminants and horses published by the World Association for the Advancement of Veterinary Parasitology (WAAVP) is a failure to reduce faecal nematode egg count by at least 95% [3]. Technically accurate definition is that resistance is a genetically determine decline in the efficacy of an anthelmintic against a population of parasite that is susceptible to the drug. Persistence and initial efficacy of the drugs were found to be far more important in determining the rate of selection for resistance as drug efficacy declined, than was the selection of resistant third larval stage parasites [4]. The challenge to veterinarians and producers is to utilize known and emerging technologies to control exposure to infection and reduce the use of anthelmintics to control GI nematodes.

2. Prevalence of Anthelmintic Resistance
The history of parasite resistance to anthelmintics starts with the first report on phenothiazine resistance in 1957. *H. contortus* was the first nematode to develop resistance against the different anthelmintics. Benzimidazoles are the oldest class of authorized anthelmintics; thiabendazole was introduced in the 1960s. The first report of decreased efficacy of thiabendazole against *H. contortus* strains dates from 1964, just 3 years after its introduction to

the market [5] (Table 1). The problem of anthelmintic resistance in GI nematode of Ruminant is worldwide and well documented reports of anthelmintic resistance have been made from South Africa, Australia, New Zealand, Malaysia, Spain, France, Denmark, UK, Brazil, and the United States [13]. In India, the first report of anthelmintic resistance in *H. contortus* to phenothiazine and thiabendazole in sheep from State Sheep and Wool Research Station, Pashulok, Rishikesh, U.P. (now in Uttarakhand) was by Varshney and Singh [14]. The prevalence of anthelmintic resistance in India is presented in Table 2.

Table 1: Introduction of anthelmintic drugs for ruminants and the development of resistance to the drug

Anthelmintic	Mode of action	Mechanism of resistance	Generic drug name	Introduced on the market	Resistance reported	Reference
Benzimidazole	Inhibiting polymerization of microtubules	Altered target structure (β-tubulin isotype 1 mutations) β -tubulin isotype 2 mutations, deletion, Altered metabolism and/or uptake	Thiabendazole Albendazole	1961 1972	1964 (USA, 1964 *H. contortus*) 1983	[6] [7]
Imidazothiazoles	Agonist of nicotinergic	Changes in nicotinic acetylcholine receptors-	Levamisole	1970	1979 (Australia, 1976 *H. contortus*)	[8]
Tetrahydopyrimidines	Acetylcholine receptors	-	Pyrantel	1974	1996	[9]
Macrocyclic lactones	Allosteric modulators of the glutamate-gated chloride channels	Mutations in GluCl and/or GABA-R genes Overexpression of P-glycoproteins Altered target (structure of Glu Cl channel & subunits)	Ivermectin	1981	1988 (S. Africa, 1987 *H. contortus)*	[10]
Amino- acetonitrile derivative	Allosteric modulator of AchR (MPTL-1), agonist	-	Monepantel	2009	2013 (New Zealand, *Teladorsagia circumcincta* and *Trich ostrongylus colubriformis)*	[11]
Spiroindol	Interfere, b-subtype, nAchR, antagonist	-	Derquantel	2010	2011 (New Zealand, *H. contortus*)	[12]

Table 2: Prevalence of Anthelmintic Resistance in India

Anthelmintic	Generic drug name	Host	Species	Place	References
Benzimidazole		Sheep	Strongyles	Karnataka	[15]
		Goat	*H. contortus*	Uttar Pradesh	[16]
		Horse	Equine Cyathostomins	Uttar Pradesh	[17]
		Goat	Strongyles	Kerala	[18]
		Goat	Strongyles	Madhya Pradesh	[19]
		Sheep	*H. contortus* and *Teladorsagia* spp.	Tamil Nadu	[20]
	Albendazole (ALB)	Sheep	*H. contortus*	Rajasthan	[21]
		Sheep	*H. contortus*	Tamil Nadu	[22]
		Goat	Strongyles	Gujarat	[23]
		Goat	Strongyles	Chhattisgarh	[24]
	Fenbendazole	Sheep	*H. contortus*	Haryana	[25]
		Goat	*H. contortus*	Haryana	[26]
		Sheep	*H. contortus*	Haryana	[27]
		Sheep	*H. contortus*	Tamil Nadu	[22]
		Goat	Strongyles	Madhya Pradesh	[28]
	Mebendazole	Goat	*H. contortus*	Haryana	[26]
Tetrahydopyrimidines	Closantel	Sheep	*H. contortus*	Tamil Nadu	[22]
	Morantel	Goat	*H. contortus*	Haryana	[25]
		Sheep	*H. contortus*	Haryana	[27]
Imidazothiazoles	levamisole (LEV)	Goat	*H. contortus*	Haryana	[26]
		Sheep	*H. contortus* and *Teladorsagia* spp.	Tamil Nadu	[29]
		Sheep	*H. contortus*	Haryana	[27]
		Goat	Strongyles	Madhya Pradesh	[28]
		Goat	Strongyles	Gujarat	[23]
		Goat and Cattle	Strongyles	Chhattisgarh	[24]
Macrocyclic lactones	Ivermectin (IVM)	Goat	Strongyle	Gujarat	[23]
		Goat and Cattle	Strongyles	Chhattisgarh	[24]
		Sheep	*H. contortus*	Haryana	[27]

3. Mechanism of development of anthelmintic resistance

The development of anthelmintic resistance is a complex theme and many factors are involved in the process of resistance selection. In general, anthelmintics are used at an efficacy of around 99.9 % against susceptible strains. The few numbers of surviving worms, which are the most resistant

component of the population, then infect the pasture with resistant offspring for next generations. There are following three intrinsic phases in the selection process which are linked to the accumulation of resistant alleles:-

Susceptibility Phase: When the frequency of resistant individuals within the population is low and occurs when the anthelmintic was used initially.

Intermediate Phase: It develops following continued exposure to a drug where the frequency of heterozygous resistant individuals within the population increases.

Resistant Phase: It is an outcome of sustained selection pressure where homozygous resistant individuals predominate within the population.

The speed of this process will depend on how severe the selection pressure is on the parasite population. Under-dosing, which is a common problem, is likely to favour the survival of heterozygous individuals, possibly enhancing the selection pressure for resistance [30].

4. Factors contributing to development of anthelmintic resistance

The rate of development of anthelmintic resistance is influenced by biological, environmental and managemental factor.

4.1 Biological factor: Parasites have short generation time and a well high prolificacy. So there is high increase in generation with spread of resistance alleles in the population. Therefore, their life cycle contributes resistance. Frequent treatments are instituted to control highly pathogenic worms subjecting them to higher selection pressure resulting in quick emergence of anthelmintic resistance. Similarly, hypobiotic worms escape the exposure of drug and contribute greatly to refugia population.

4.2 Environmental factors: Climatic conditions determine the type of parasites prevalent and propagate in a particular area. Heavy worm burden during wet season may require higher anthelmintic intervention and this can select rapidly for resistance.

4.3 Managemental factors: Managemental factors are found responsible for emergence of anthelmintic resistance at higher rate.

4.3.1 Drench frequency: It has been observed that frequent usage of the same group of anthelmintic may result in the development of anthelmintic resistance [31].

4.3.2 Under dosing: Under dosing is generally considered an important factor in the development of anthelmintic resistance because sub therapeutic doses might allow the survival of heterozygous resistant worms [32].

4.3.3 Continuous use of drug with similar mode of action: 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 [33].

4.3.4 Targeting and timing of mass treatment: Prophylactic mass treatments of domestic animals have contributed to the widespread development of anthelmintic resistance in helminths. Computer models indicate that the development of resistance is delayed when 20% of the flock is left untreated but it needs confirmation through experimentation [34].

5. Detection methods of anthelmintic resistance

Resistance cannot be measured on the basis of an apparent clinical failure to anthelmintic treatment. Other reasons could make clinical signs similar to those normally associated with nematode diseases. Therefore, detection methods are an important means to prove if resistance to an anthelmintic compound is true. Different *in vivo* and *in vitro* tests are now available and there is an ongoing effort to refine, standardize and validate these tests [35].

Table 3: Bioassays for the detection of anthelmintic resistances

A. *IN VIVO* Tests	**Detection of resistance to**	**Application**
1. FECRT (Faecal Egg Count Reduction Test)	All	Widespread
2. Controlled Slaughter Test	Anthelmintic	Limited
B. *IN VITRO* Tests		
1. Egg Hatch Assay	BZ/LEV/MT Levamisole/Morantel	Widespread
2. Larval Paralysis Assay	Benzimidazoles	Limited
3. Tubulin Binding Assay	All drugs	Limited
4. Larval Development Assay	Benzimidazoles	Commercialized
5. Adult Development Assay	All drugs	Limited
6. Molecular Based Test		Limited

5.1 Faecal egg count reduction test. (FECRT): This is the most common test to study anthelmintic resistance. The ability of the anthelmintic in question to reduce the concentration of eggs per gram of faeces (EPG) by more than 95 percent, measured 10-14 days after treatment, in comparison with the EPG measured at the time of treatment. Failure to do so is indicative of resistance. This test was originally designed for sheep, but can be used also for cattle, swine and horses. Cut-off value for drug efficacy in FECRT 95% and 90%, macrolides and benzimidazoles / pyrantel, respectively.

5.2 Controlled slaughter test: In this test, the efficacy of an anthelmintic is determined by comparing parasite populations in groups of treated and non-treated animals. Basically, the procedure compares worm burdens of animals artificially infected with susceptible or suspected resistant isolates of nematodes.

5.3 Egg hatch assay: It is based on the determination of the proportion of eggs that fail to hatch in solutions of increasing drug concentration in relation to the control wells, enabling the user of the test to develop a dose response line plotted against the drug concentration. The reference drug used to conduct this test is thiabendazole.

5.4 Larval Paralysis: This assay discriminates between resistant and susceptible strains of parasites, by estimating the proportion of third stage larvae in tonic paralysis after incubation with a range of levamisole and morantel drug

concentrations.

5.5 Tubulin Binding Assay: The test is based on the differential binding of benzimidazoles to tubulin, an intracellular structural protein from susceptible and resistant nematodes. Tubulin binding assay involves the incubation of a crude tubulin extract from adult parasites, infective larvae or eggs, with a titrated benzimidazole until equilibrium is reached.

5.6 Larval Development Assay (LDA): Nematode eggs are isolated from a faecal sample, placed into wells of a microtitre plate and allowed to develop through to infective L_3 larvae in the presence of a range of concentrations of anthelmintic. The LDA is detection of resistance to benzimidazoles, levamisoles and macrocyclic lactones in nematodes parasites of sheep, horses, pigs and cattle.

DrenchRite® Kit Larvae development assay developed and marketed as DrenchRite® kit (Horizon Tech, Australia) claimed as most suitable *in vitro* detect anthelmintic resistance among all major broad spectrum anthelmintics.

5.7 Adult Development Assay: The adult development assay for detecting benzimidazole resistance in trichostrongylid nematodes has advanced significantly and *H. contortus* has been cultured through to the adult egg-laying stages, although this test is mainly for research purposes.

8. Molecular Based Tests: The most common molecular mechanism that confers benzimidazole resistance in trichostrongyles in small ruminants involves a phenylalanine to tyrosine mutation at residue 200 of the isotype 1 β-tubulin gene. However, in addition a similar mutation at codon 167 may be involved in benzimidazole resistance in nematodes. An allele-specific polymerase chain reaction (AS-PCR) has been used to detect this mutation in *H. Contortus* and *Teladorsagia circumcincta* adult and larval stage [41].

6. Management strategies to delay the development of resistance

The key areas of concern in the management of anthelmintic resistant throughout the world are: a. Drug related factors (pharmacokinetics, formulation and mode of application of anthelmintics). **b.** Management related factors (incorrect dosing of anthelmintics, frequency of anthelmintic treatment, and use of the same anthelmintic class for several years, pasture management of livestock). **c.** Parasite related factors (number of nematodes in refugia, frequency of genes for resistance in an unselected parasite population, genetic factors as mode of inheritance, fitness and fecundity of resistant nematodes, generation time).

6.1 Treatment Strategies

6.1.1 Correct use of anthelmintics: Under dosing and/or too frequent use of anthelmintics belonging to the same class will increase the risk for selection of resistance [42].

6.1.2 Reduction in frequency of treatment: Selection occurs at faster rate with increasing frequency of treatment due to high selection pressure.

6.1.3 Rotational use of anthelmintic: From the experiment on the frequent use of the same anthelmintics, it has been demonstrated that the alteration of the anthelmintic family may slow down the selection of benzimidazole resistant worms during early steps of resistance development [43].

6.1.4 A combination drug strategy: Treating simultaneously with 2 drugs from different anthelmintic classes is one method of preventing the development of anthelmintic resistance.

6.1.5 Using optimum dose: Under dosing occurs when a host is administered a weight-dependent dose that is less than recommended by the manufacturer and it results from misestimating of body weight. Proper check must be done for calibration of drenching device.

6.1.6 Regular monitoring of anthelmintic resistance: Regular annual testing with *in vivo* or *in vitro* test is required on farm to monitor the status of drug efficacy of anthelmintics.

6.1.7 Targeted selective treatment (TST): Targeted selective treatment can be defined as any system that selects animals on an individual basis for treatment, using logical specific criteria on which this selection is made. One in which only those animals that will most benefit from treatment are given anthelmintic. For TST to be viable there must be practical tools that producers can use to make deworming decisions the first tool developed was the FAMACHA system, the Five Point Check is an extension of the FAMACHA system. In the TST group, only 20% of the flock required treatment at any one time and moreover 88% of the animals that were given anthelmintic showed a positive response in performance following treatment [44].

Table 4

Check point	Observation	Possibilities
1. Eye	Anaemia, 1-5 (FAMACHA© card) (3-5)	*Haemonchus,* Liver fluke, Hook worms and other diseases
2. Back	Condition score 1–5 (BCS card) (1-2)	*Teladorsagia, Trichostrongylus, Oesophagostomum,* and other worms
3. Tail	Faecal soiling 1-5 (Dag score card) (3-5)	*Teladorsagia, Trichostrongylus, Oesophagostomum,* Flukes and other worms
4. Jaw	Soft swelling	*Haemonchus,* liver fluke Hook worms and other diseases
5. Nose	Discharge	*Oestrus ovis,* Lungworms and other

6.2 Alternative anthelmintic treatments

6.2.1 Copper-Oxide Wire Particles: Non-chemical strategies to control internal parasites in animals, with these introduced non-chemical approaches form the framework for the livestock health and welfare regarding parasites. The basic principal of this treatment is that the availability of macro-minerals and trace elements influences the host-parasite relationship [45]. When copper-oxide wire particles (COWP) are administered they remain in the rumen and release free copper into the abomasum this free copper particle creates an environment that affects the establishment of *H. contortus* in the abomasum. Copper oxide is available for cattle as a supplement to copper deficiency and has been used in sheep for the same purpose. Optimal dosage is 0.5-2gm as a single

dose to be sufficient to result in reduced FEC [46]. Other chemicals which are having similar activity are diatomaceous earth (DE), copper sulphate and nicotine sulphate.

6.2.2. Use of herbal anthelmintic: Plants or plant parts with anthelmintic activity are used in folk veterinary medicine, but it is necessary to investigate and scientifically validate low-cost phytotherapeutic alternatives for future use to control GI nematodes in animal by farmers. Indigenous plants like *Areca catechu, Artemisia vulgaris, Calotropis procera, Calotropis procera, Melia azadarach, Chrysanthemum* spp., *Carica papaya, Heracleum* spp., *Azadirachta indica, Allium sativum, Heyysarvum coronarium, Artemisia maritime,* etc showed potential anthelmintic activities against nematode parasites [47].

7. Immunological approaches: Several natural antigens have been used to develop protection through vaccination but none have been mass produced. Vaccines have been developed to the "hidden" antigens and "natural" antigens. Hidden antigens are those which do not cause a detectable immune response in the host with natural infections and are thought to be internal antigens of the nematode. The first most effective vaccine against a GI parasites was Barbervax against *H. contortus*, release in October 2014. A "hidden" antigen vaccine Barbervax can be use for lambs, 5 subcutaneous injections of 1 ml, at approximately 6-week intervals (David Smith Moredun Research Institute, Edinburgh, UK). Some effective antigen which are under trial period are H11 (*H. contortus*), Tropomysin 41 (*Trichostrongylus columbriformis*) and ES31 (*Oestertagia circumcincta*) in sheep.

8. Biological control: Bio-control agent's origin may be from plants like grasses, or from zoological origin like bacteria, fungus, virus, parasite and predator. Fungi that exhibit anti nematode properties have been known for a long time. They are divided into three major groups based on their morphology and types of nematode destroying properties. The first the group the predacious fungi produces specialized nematode-trapping structures (adhesive knobs, networks, rings etc.) on the mycelium. The species of predacious fungus which has received most attention recently is *Arthobotrys* spp. (*A. oligospora*) and *Monacrosporium* spp. [48]. The second group, the endoparasitic fungi, produce spores which either by penetration of cuticle from sticky spores adhering to the cuticle or following ingestion of spores which lodged in the gut. Examples of endoparasitic fungi are *Drechmeria coniospora* and *Harposporium anguillulae* [49]. The third group the egg parasitic fungi have the ability to attack the egg stage and may have a role in the control of animal parasites which have a long development and/or survival time in the egg stage in the environment outside host. Eggs of *Ascaris lumbricoides* collected from naturally infected pigs were used mainly to test the effect of the fungus *Verticillium chlamydosporium* but also other *Verticillium* spp. the fungus was shown to be able to degrade the egg shell enzymatically and infect the eggs [50].

9. Nutritional Management: The strongest link between nutrition and parasitism has been illustrated between protein intake and resistance to GI nematode infection. Animals on low protein diets are more susceptible to infection because they produce less IgA (immunoglobulin). Minerals (Cu, Zn, Fe, Cobalt, phosphorus) and Vitamin supplements (A, B_{12}, E) amount a better immune response to internal parasites. Surprisingly, addition of molybdenum at 6-10 mg Mo/day decreased worm burdens in lambs that were not attributable to the expected copper deficiency. Molybdenum may have a role in increasing jejunal mast cells and blood eosinophils numbers [51].

10. Genetics Management: It is best long term weapon against internal parasites as some breeds are more resistant and resilient to internal parasites. Selection for parasite resistance breed is possible and will not adversely affect growth of animals. Recent years breeding policy has more concentrated on the development of parasites resistance breed. Parasites trait is moderately heritable 20-40 per cent [52]. Grazing resistant breeds with susceptible breeds, may act to "sweep" pastures and reduce contamination to susceptible animals. Some breeds which are resistance against GI nematodes; Red Masai sheep, Florida Native Sheep, St. Croix Sheep, Galore and Barbados Back belly.

11. General management: Parasite control starts with good management and common sense. Animal should not be fed on the ground. Water should be clean and free from faecal matter. Facilities of proper drainage in the anima shed reduce the chance of survival of the parasites, Pastures and pens should not be overstocked. When new animal are acquired they should be isolated from the rest of the flock for days and aggressively dewormed to prevent the introduction of drug-resistant worms.

11.1 Use of clean or safe pastures: Safe pastures means the pasture which are not contaminated with the worm larvae and clean pastures means the pasture which are not been grazed by sheep or goats for the past 6 to 12 months but by horses or cattle. Hay or silage crop has been removed. Rotated with field crops. Burning a pasture will remove worm larvae.

11.2 Pasture rest and rotation: Resting period varied from 2 months (semiarid) to 6 months (cool moist climate) but 60- 65 day rest period is sufficient. In rotational grazing system ideally, sheep/goat should not be returned to the same pasture for 2-3 months.

11.3 Alternate grazing system/ Graze multiple species: Grazing between different age group of different species taking each species has different grazing behaviour that complements one another. Cattle /horse act as vacuum cleaner to the pasture if grazed before or after sheep/goat. Pastures grazed by cattle and horses are safer for sheep/ goats (Area where *T. axei* is not a major problem). Sheep/goat does not graze together on same pasture.

11.4 Grazing strategies: Stocking rate is an important consideration in parasite control as it affects exposure to infective larvae and contamination of the pasture. Thumb rules include 5–7 goats or 5 sheep being the equivalent of 1 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.

11.5 Zero grazing: Keeping animal in confinement (i.e. "zero grazing") is a means of reducing parasitism and preventing re-infection. Under a zero grazing situation, animal does not have access to any vegetation for grazing.

11.6 Use of bioactive forages: The pasture plants containing condensed tannins have anthelmintic properties [53]. Condensed tannins (CT) are not only included in certain plants, a lot of plants have CT content but only those with higher levels are referred to as 'bioactive forage'. Some examples of bioactive forages are Chicory, Birdsfoot Trefoil, Sulla, Sainfoin, Quebracho etc.

11.7 Community dilution: The only option that holds promise for practical application in the field is to engineer reversion by overwhelmingly diluting resistant worms with susceptible worm strains.

11.8 Refugia: It means the proportion of the worm population escaping exposure to anthelmintics. Most parasitologists now consider level of refugia as the single most important factor contributing to selection for anthelmintic resistance in parasites [54]. The size of population in refugia at the time of anthelmintic treatment will determine the contribution of surviving worms to the subsequent generation and this was presented as a major source of resistance. Worms in refugia provides a pool of genes susceptible to anthelmintics, thus diluting the frequency of resistance genes. As the relative size of refugia increases, the rate of evolution towards resistance decreases. The density of parasite in refugia plays a major role in augmenting the rate of development of anthelmintic resistance.

11.9 Bioclimatographs: Bioclimatographs are used to predict the effect of climate on epidemiology of nematodes. Bioclimatograph are graphs in which total Meteorological data including temperature (maximum and minimum), average relative humidity and total rainfall recorded for each month and correlated with faecal egg count, faecal larval count and pasture larval count of grazing area. Resultant points are joined in a closed curve. Bioclimatographs are climatographs on which line indicating the limits of the climatic condition most favourable for the propagation of life, in this case free living stage of ruminant nematodes superimposes.

11.10 Use of computer models: Recent developments in computer modelling, following comprehensive investigations into the population dynamics of parasites both within the host and on pasture, will be great benefit in evaluating new control schemes. FROGIN (Forecasting for the Rajasthan Ovine Gastrointestinal Nematodosis) is a computer based mathematical modelling for forecasting of *H. contortus* in sheep in Rajasthan. Some countries developed parasite control decision trees like sites http://wormboss.com.au in Australia and New Zealand, www.weide-parasiten.de in Turkey and www.parasietenwijzer.nl in Netherland.

12. Conclusion

Parasites are a major cause of disease and production loss in livestock, frequently causing significant economic loss and impacting on animal welfare. In addition to the impact on animal health and production, diagnosis and control measures are costly and often time-consuming. A major concern is the development of resistance by worm to many of chemical used to control them. Therefore is a urgent need for development of early detection methods along with planned preventive programs to minimize the risk of parasitic disease outbreak and sub clinical losses of animal production. Some techniques must be used such as smart drenching, FAMACHA, the five point check and increased housing management which can help to manage parasites. These techniques reduce dependence on dewormers and lead to a more sustainable parasite-management program. Integration of more than one measure like good farming practices, best breeding strategies, nutritional management, appropriate herbal anthelmintic, biological, immunological control measures, scientific utilization of biotechnological tools, mathematical models, decision support system and appropriate chemical control measures is essential to achieve the sustainable control on the parasites.

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