Anthelmintics Resistance on Goat Gastrointestinal Nematodes
(Case Study in Arero District, Southern Ethiopia)

Gerade Abduljami

Gerade Abduljami
Arero District, Southern Ethiopia

Abstract: A study was conducted to assess the development of anthelmintic resistance by gastrointestinal nematodes from January 2018 to July 2018 in Arero district, Southern Ethiopia. After agreements were made with the owner of goats in Arero, the fecal samples of traditionally managed and naturally infected of 384 goats were directly collected from the rectum, the eggs of parasite were counted by using the modified McMaster technique and the result was recorded using the owner’s name with the animal name which given depend on body mark, gift and their behavior, for ease of identification. This study was conducted using faecal egg count reduction test (FECRT). For the study eighty goats of both sexes and aged from six to eighteen months with faecal egg count (FEC) of more than 150 eggs per gram of faeces were selected for the field experiment. The animals were grouped in to Albendazole, Tetramisole, Ivermectin and control groups randomly. From a total of 384 goats faecal sample taken during the screening 201(52.3%) of the goats were shedding gastrointestinal nematodes eggs. Faecal samples were collected on day 0 before treatment, and again on day 12 post treatment. Efficacy of all the drugs was assessed on day 12 post treatment by faecal egg count reduction test (FECRT). Multiple anthelmintic resistances in nematodes against Albendazole and Ivermectin were recorded in all age categories of the goats. However tetramisole showed good efficacy against nematode in this area. However, large scale studies are needed to assess the current status of anthelmintic resistance against the most commonly used anthelmintics in different agro ecology, species of animals and management systems in Ethiopia.

Keywords: Anthelmintics resistance, faecal egg count, gastrointestinal nematodes, goats, albendazole

1. INTRODUCTION
Small ruminant production is important due to the fact that it can easily be managed, requires small initial investments and its short generation interval (Otte, M.J. and P. Chilonda. 2002). Goats are widely distributed in all climatic zones but with a high concentration in dry areas. This is because they are well adapted to hot and dry conditions and mainly to the fact that in dry zones there is less opportunity for alternative land use (ILCA, 2013). The estimated number of sheep in Ethiopia is about 25.02 million out of which about 73.38 percent are females, and about 26.62 percent males. The number of goats reported in the country is estimated to be about 22.6 million. Out of these total goats, about 69.84 percent are females and 30.16 percent are males (Nizam, 2013). A 2013/2014 livestock
census puts the goat population in Ethiopia at 22.6 million (CSA, 2013) of which 32% goats were found in Oromia Regional State. Ethiopia is known to have a high population of sheep and goats. Majority of Ethiopian goat farmers are subsistence farmer. In southern zone large number of goats and Small ruminant used for the community as source milk, meat, cash income, skin, manure and employment for family member (Bedane et al., 2009). Several previous studies conducted in different parts of Ethiopia indicate that gastrointestinal nematodes in goats are very common and widespread in all livestock systems in the country (Kumsa and Wossene 2006a; Sissay et al., 2006a; Thomas et al., 2007).

The most commonly reported adverse effects of gastrointestinal nematodes in goats include: low productivity, decreased weight gain, un thriftiness, delay in puberty, anorexia, hypoproteinemia, loss of meat and wool, impaired digestive efficiency, organ condemnation, poor reproductive performance, and death of severely infected animals (Tembely et al., 2001). Anthelmintic have a pivotal role in minimizing the negative effects of nematodes worldwide. However, indiscriminate and frequent use of these drugs has resulted in the emergence of anthelmintic resistance against most of the major classes of anthelmintics in several countries (Coles et al., 2006; Jabbar et al., 2006, and Saeed et al., 2007). Anthelmintic resistance in nematodes of small ruminants has been reported from different parts of the world (Cringoli et al., 2007, and Saeed et al., 2007). In Ethiopia, the use of anthelmintics in helminth control is known and has been going on for a quite long time, taking a considerable share in drug costs. Smuggling and improper use of veterinary drugs including anthelmintics is a widespread practice in the country. Although, anthelmintics are very commonly used in Ethiopia, and despite the great variety of drugs circulating in the market legally or illegally, almost no efficacy trials are conducted in proper and regular manner (Sissay et al., 2006b). Despite the great importance and considerable time of use of anthelmintics in Ethiopia, limited numbers examining the efficacy of these drugs are reported (Asmare et al., 2005; Kumsa and Wossene 2006b, and Sissay et al. 2006b). This implies that the extent, prevalence and economic significance of anthelmintic resistance in the country are not known.

Control of gastrointestinal nematode parasites of livestock in smallholder farmer and agro ecologies is done with limited anthelmintic drug use, or with traditional herbal remedies, and is performed mainly during the rainy seasons (Miller and Waller, 2004). However, for smallholder farmers and stock owners in rift valley, drugs are relatively expensive and are often not easily accessible, while frequent and indiscriminate use of different classes of anthelmintics has been reported in institutional and large commercial farms in Ethiopia (Sissay et al., 2006a). With the advent of helminthes parasite populations that have developed resistance to anthelmintics over the last decade. Especially in small ruminants, livestock productivity has been threatened worldwide (Miller and Waller, 2004). The Study will be conducted to investigate the status of anthelmintic resistance in goat flocks maintained as separate operations at pastoral area, located Arero district.

Therefore, the objective of this study was to investigate the existence of GIT resistance for mostly used Albendazole, Tetramisole and Ivermectin brand, in naturally infected goats under field conditions in the pastoral area, located Arero district in southern Ethiopia.

2. LITERATURE REVIEW
2.1 Anthelmintic drug

Anthelmintics are drugs that are used to treat infections with parasitic worms. This includes both flat worms, flukes and tapeworms and round worms, i.e. gastrointestinal nematodes are one of the most important causes of losses in productivity of goats in Ethiopia. Economic losses incurred by nematodes include reduction in weight gain, low fertility, reduced performance, condemnation of organs, cost of treatment and mortality in severely infected cases. Several previous coprological and abattoir studies conducted in different parts of Ethiopia indicate high prevalence and wide distribution of gastro intestinal nematodes in goat (Kumsa and Wossene, 2006a). Owing to lack of sound management strategies against helminthes of livestock in any of the agroecologies in Ethiopia, control of adverse effects of nematodes on grazing ruminants relies almost exclusively on the use of anthelmintic. Despite the prevalence of parasitic worms, anthelmintic drug discovery is the poor relation of the pharmaceutical industry. The simple reason is that the nations which suffer most from these tropical diseases have little money to invest in drug discovery or therapy. It comes as no surprise therefore that the drugs available for human treatment were first developed as veterinary medicines.
some respects, this situation has been exacerbated by the remarkable success of Ivermectin over the last twenty years, which has decreased motivation for anthelmintic drug discovery programmes (Harder, 2002). This prompts concern, as anthelmintic resistance has been widely reported in livestock and it may also only be a matter of time before this phenomenon occurs in parasites of humans. There is large range of formulation and substances from which to choose (Boden, 2005). Many highly effective and selective antis parasitic are available to obtain a favorable clinical response, accomplish good control, and minimize selection for anthelmintic resistance (Harder, 2002).

The ideal Anthelmintic should have broad spectrum activity against mature and immature parasite (including hypo biotic larvae), be easy to administer, inhibit reinfection for extended period of time, have a wide margined of safety and be compatible with other compounds, not require long with holding period and cost effective (Radostits et al., 2007). Antiparasitic must be selective toxic to the parasites. This is usually achieved either by inhibiting metabolic process that is vital to the parasite but not to host or by inherent pharmacokinetic properties of the compounds that cause the parasite to be exposed to higher concentration of the antiparasitic than are the host cells. The pharmacological basis of treatment for helminthes generally involves protective mechanism against host and immunity, which lead to starvation, paralysis expulsion of the parasites by two major mechanisms: 1. They interfere with energy generating metabolism causing death by starvation and 2. Interfere with neuromuscular transmission in nematodes causing paralysis (Kahn and line, 2005). Antiparasites are administered to animals by variety of methods and formulations, the three common route of administration are oral, injection and topical (Harder, 2002).

2.1.1. Pharmacokinetics

After administration ant parasites are usually absorbed into the blood stream and transported to different parts of the body including liver where they may be metabolized and eventually excreted in feace and urine. Intestinal parasite comes in contact not only with the unabsorbed drug passing the gastrointestinal tract but also any that is recycled into the gut (Kahn and line, 2005).

2.1.2 Major Anthelmintics drugs

Many broad spectrum anthelmintics are now available that combine high efficacy against larval and adult worms with low toxicity in sheep, goats, and cattle. Most however belong to just three major chemical groups namely: benzimidazoles, imidazathiazoles and macrocyclic lactones (Urquhart et al., 1996, 2006, Radostits et al., 2007).

2.1.2. a. Benzimidazole

Benzimidazoles are group of broad spectrum anthelmintic drugs with high degree of efficacy and good margin of safety and similar mode of action. The disrupt energy metabolism of parasites by binding to tubules, a protein required for uptake of nutrient in the parasites (Kahn and line, 2005). Benzimidazoles are large chemical family used to treat nematodes and trematodes infection in domestic animals. However, with the wide spread development of resistance and availability of more efficiently and easier to administer compounds, their use is rapidly decreasing. Benzimidazoles of interested are: Albendazole, Fenbendazole, Thiabendazoles, Triclabendazole, Mebendazole, Oxfendazole, Oxibendazole and Febantel (Radostits et al., 2007). Because of most benzimidazoles are sparingly soluble in water they are given oral as suspension, paste and bolus. Difference in the rate and extent of absorption from gastrointestinal tract is depending on such factor as species, formulation and solubility. The most effective of the group are those with the longest half-life such as Oxfendazole, Fenbendazole, and their pro drug, because the nature of their antiparasitic action depends of prolongation of contact time (Albnico, 2003, Kahn and Line, 2005, Entrocasso et al., 2008). In ruminant oral treatment with the benzimidazoles removes most major adult gastrointestinal parasites and many of larval stages. The relative rate of oxidation in the liver and reduction in the gastrointestinal tract vary between cattle and sheep, with the metabolism and excretion of benzimidazoles compound being more extensive in cattle are often higher than those in sheep (Radostits et al., 2007, Entrocasso et al., 2008).

Albendazole is a broad spectrum anthelmintic for the treatment of intestinal helminth infections. It also hydatid activity and is recognized to have important application in treatment of human cystic
and alveolar echinococcosis. Kahn and Line (2005) reported that albendazole is a potent member of benzimidazole (BZS) group of anthelmintics, with a wide range of activity against GIT round worms including inhibited larval stages, tapeworms, liver fluke and lung worms in many species. It blocks glucose uptake in the larval and adult stages of susceptible parasite, there by depleting the energy stores and decreasing formation of ATP leading to immobilization and death of the parasite (Harder, 2002).

Following oral administration, Albendazole is rapidly absorbed and cannot be detected in plasma, because the drug is quickly metabolized in liver mainly to albendazole sulfoxide and a lesser extent, to other metabolites (Marriner et al., 2001) About 3 hours after oral administration, the sulfoxide attains its maximum plasma concentration. The metabolites are mainly excreted in the urine and only a small amount is excreted in the feces. Albendazole is absorbed to a much great degree than the other BZS because 47% of the administered dose is recovered in urin over a 9-day period (Marriner et al., 2001).

2.1.2. a. Imidazothiazoles

Imidazothiazoles are groups of anthelmintics drugs effective against round worm the group acts by interfering with parasitic nerve transmission causing muscular paralysis effective against adult and larval gastrointestinal round worm and lung worm infectious including Protostrongylus infections. Most worms are expelled within 24 hrs of administration of the drugs (Harder, 2002, Radostits et al., 2007). The commonly used drugs belonging to this family are tetramisole and levamisole. These drugs act on round worms, nerves system as cholinergic agonist thereby causing paralysis and expulsion of the parasites (Radostits et al., 2007). It is commonly used in cattle, sheep, pigs, goats and poultry to treat nematode infections. It is normally administered oral and sc. Efficacy is generally considered equivalent with either route (Urquhart et al., 2003 Upadhayay, 2005). In ruminant, levamisole or tetramisole is highly effective against the common adult GIT nematodes and lung worm (Upadhayay, 2005).

2.1.2. c. Macrocyclic lactones

Macrocyclic lactones are compounds derived from fermentation products of soil dwelling bacteria of genes streptomycin. The product is active against both GI round worms and ectoparasites of animals when used at lower concentration (Kahn and Line, 2005). The macrocyclic lactones are well absorbed when administered oral, Parenteral or as pour on formulation. Regardless of the route of administration macrocyclic lactones are extensively distributed throughout the body and concentrate particularly in adipose tissue. Effective levels are reached in the GI system, lung and skin regardless of route of administration (Kahn and Line, 2005). The macrocyclic lactones in commercial use are ivermectin, abamectin, doramectin, eprinomectin and selamectin. They are active against many mature and immature nematodes, and arthropods. The macrocyclic lactones have a very high efficacy against all stages including in active forms of the common cattle, sheep, and goats nematodes. The least susceptible nematodes are cooperies and Nematodirus species (Radostits et al., 2007). The macrocyclic lactones bind to glutamate-gated chloride ion channels in invertebrate nerve and muscle cells. The cell membranes then develop an increased permeability to chloride ions causing hyperpolarization of affected cells and subsequent paralysis and death of the parasite. Medications in this class also interact with other ligand gated chloride channels, including ones gated by gamma aminobutyric acid (GABA).

Because mammals do not have glutamate-gated chloride channels and macrocyclic lactones have a low affinity for other mammalian ligand-gated chloride channels, mammals have low susceptibility to the effects of macrocyclic lactones. Also, these medications are slow to penetrate the blood brain barrier (BBB), protecting the GABA gated channels in mammalian central nervous systems (Kahn and Line, 2005).

Ivermectin activate the chloride channel, causing an inhibitory effect, which when excessive results in paralysis and death of the parasite. The rout of administration for ivermectin is Subcutaneous. Minor differences in vehicle may alter the bioavailability of subcutaneously administered ivermectin. One study showed significant variations in absorption, peak plasma concentration, and mean residence time among generic ivermectin injection productions (Radostits et al., 2007).

The predominant route of elimination for the macrocyclic lactones is by excretion through bile into the feces (50 to 96% of the dose), primarily as unmetabolized drug. Small amounts are eliminated
in the urine (Mealey et al., 2001). Macrocyclic lactones have been marked as broad spectrum anthelmintics with most of them having effect against nematodes, insects, mites and ticks. Therefore, they classified as anthelmintic, insecticides and acaricides (Kahn and Line, 2005).

2.2 Anthelmintics Resistance

Anthelmintic resistance is defined as a decrease in the efficacy of an anthelmintic against a population of parasites that is generally susceptible to that drug the extensive use of anthelmintic for control of helminthes infection on grazing livestock has resulted in the development of resistance that has become a major practical problem in many countries resistance in the field is usually suspected when there is an apparent poor clinical response to anthelmintic treatment (Taylor et al, 2002).

This decrease in susceptibility is caused by an increase in the frequencies of “resistance” gene alleles that result by selection through repeated use of an anthelmintic. Gastrointestinal nematodes of small ruminants have a number of genetic characteristics that promote the development of anthelmintic resistance. Among the most important of these features are: (1) rapid rates of nucleotide sequence evolution and extremely large populations resulting from the high fecundity of each individual nematode, providing an exceptionally high level of genetic diversity (Leathwick, 2012) and (2) a population structure consistent with high levels of gene flow (dissemination), suggesting that host movement is an important determinant of nematode population genetic structure. As a result, these helminths have the genetic potential to respond rapidly and successfully to chemical attack and the means to ensure dissemination of their resistant genes by host movement from farm to farm (Taylor et al, 2002).

The problem of anthelmintic resistance in gastrointestinal nematodes of small ruminants is worldwide. In the past 25 years, no new classes of anthelmintics have been developed for use in animals, and given the limited economic potential of small ruminant production; there is little interest in pursuing licensing of anthelmintics for this group of animals. Currently, there are 3 classes of anthelmintics commonly used in small ruminants: benzimidazoles (including albendazole, fenbendazole), cholinergic agonists (including levamisole/morantel), and the macrocyclic lactones or ivermectins and milbemycins. The earliest documentation of anthelmintic resistance was to phenothiazine in 1957 followed by thiabendazole in 1964 (Sykes and Coop, 2001).

There is no anthelmintic use policy in the country as a result misuse and smuggling of anthelmintics in many forms like illegal trading in open market and irrational administration is a widespread practice. As severity of anthelmintics resistance increase in nematodes of small ruminant it is evident that no single approach remains to control the steady. Efficacy of anthelmintics is continuously constrained by many factors like under dosage, exclusive use of drugs of the same mode of action, substandard drugs and inappropriate use of anthelmintics. Demise of the available anthelmintics. Anthelmintics resistance is an important consideration influencing the choice and intensity of control measures (Kahn and Line, 2005; Radostits et al., 2007).

2.3 Development of Anthelmintics Resistance

It is accepted that during anthelmintic treatments, a small number of worms survive; these being the most resistance proportion of population and these worms contaminate the pasture with majority of resistance larvae for subsequent generation, leading gradually to the selection pressure of anthelmintic resistance. This selection rate depends on the percentage contribution to the next generation between nematodes surviving after treatment and other one not exposed to it (Papadopoulos, 2008).

Parasite resistance against all important anthelmintics is a significant problem in some animals host condition such as return to infected pasture the proportion of a parasite population that is not exposed to anthelmintics during any one treatment e.g. nematode larval stages on pasture, thus escaping selection for resistance and potentially able to propagate its genes to the next generation, emergency of hypobiotic larvae, mass medication in appropriate therapy resulting in drug resistance most of the reports of anthelmintic resistance are from large scale commercial or institutional farms. Under these conditions, the selection pressure for anthelmintic resistance is often intense with, for example, frequent anthelmintic treatment of the whole herd. This in itself exposes a greater proportion of the nematode population to anthelmintics and leaves fewer worms in refugia than would be the case, for example, if only those individual animals showing signs of helminthosis were drenched (Van Wyk J A,
2001). The frequent use of anthelmintics increases the frequency with which individual nematodes and their offspring are exposed to anthelmintics as well as the probability that a nematode will be exposed to an anthelmintic within a certain period of time. Large herd size has been reported as a risk factor for the presence of resistance. Farmers with large flocks are more likely to be able to buy anthelmintics. Conversely, farmers with smaller flocks often cannot afford to buy anthelmintics and this may serve to slow down the onset of resistance (Kahn and Line, 2005, Entrocasso et al., 2008).

Various authors speculate that the occurrence of anthelmintic resistance in a flock/herd resulted from the introduction of resistant worms from other flocks/herds. This may have been through the sale or distribution of stock (together with their resistant worms) from larger commercial or government owned farms to smaller farms), through the introduction of stock from other farms (where no mention of size of farm is made), through the appropriation of farms from commercial farmers and addition to existing communal pastures; and through communal grazing (Vatta et al.; 2001). Over use chemical as deworming agent in the past lead to the development of anthelmintics resistance of gastrointestinal nematodes (Burke and Miller, 2008).

2.3.1 Generally factor lead to anthelmintics resistance

2.3.1.1. Treatment frequency

It has been observed that frequent usage of the same group of anthelmintic may result in the development of AR (Silvestre and Humbert, 2002). There is evidence that resistance develops more rapidly in regions where animals are dewormed regularly. Anthelmintic resistance in H. contortus has been reported in some humid tropical areas where 10 to 15 treatments per year were used to control this parasite in small ruminants. Drug resistance, however, can also be selected at lower treatment frequencies, especially when the same drug is used over many years and also reported the development of AR even when only two or three treatments were given annually (Silvestre and Humbert, 2002).

2.3.1.1. Under dosing

Under dosing is generally considered an important factor in the development of AR because sub therapeutic doses might allow the survival of heterozygous resistant worms (Kahn and Line, 2005). Several laboratory experiments have shown that under dosing contributes to the selection of resistant or tolerant strains. Moreover, variation in bioavailability in different host species also is crucial for making a decision about correct dose. Some indirect field evidence further supports this conclusion. For an example, the bioavailability of benzimidazole and levamisole is much lower in goats than in sheep, resultantly those goats should be treated with dosages 1.5 to 2 times higher (the single dose is much less inferior than “sub-optimal”, it is rather near half the dose necessary for goats) than those given to sheep (Hennessy, 1994). For many years, however, sheep and goats were given the same anthelmintic doses. The fact that AR is very frequent and widespread in goats may be a direct consequence of difference in metabolism of drugs (Silvestre and Humbert, 2002).

To reduce the costs of anthelmintic treatment in developing countries, the use of lower dosages than the recommended therapeutic ones has been advocated. Such practices should clearly be avoided. Most of the currently applied anthelmintics are in fact sub curative in at least part of the population. Additionally, there are a number of species of nematodes which are present as mixed infection in animals’ throughout the world which responds to different groups of anthelmintics differently due to the irregular susceptibility of these species to a given anthelmintic. This is considered acceptable for morbidity control, but in the long run such strategies may contribute to the development of AR as well (Silvestre and Humbert, 2002).

2.3.1. c. Mass treatment

Prophylactic mass treatments of domestic animals have contributed to the widespread development of AR in helminths. Computer models indicate that the development of resistance is delayed when 20% of the flock is left untreated (Van wyk, 2001) 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 helminths generation that consists almost completely of worms that survived therapy and, therefore, might contribute to the development of AR (Van wyk, 2001).

2.3.1. d. 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. In a survey of sheep farmers in Tennessee 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 helminthes 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. Development of resistance depend upon whether resistance worms are as fit, by means of life cycle completion, egg production pasture survival and infectivity or less fit than susceptible ones (Coles *et al.*, 2006; Van Wyk *et al.*, 2006; and Papadopoulos, 2008).

2.4. Detection of Resistance
Two tests are available to veterinarians for determining the presence of anthelmintic resistance in small ruminants. One is a simple test that can be performed locally, and the other requires a laboratory that specializes in this type of testing. Larval identification can be used to determine which species of parasites are resistant (Maingi *et al.*, 1998).

2.4.1. Fecal Egg Count Reduction Tests
The test most commonly used to detect anthelmintics resistance remain the faecal egg count reduction test (FECRT). It is suggested that guidelines published by the World Association for the Advancement of Veterinary Parasitology (WAAVP) be used to perform and evaluate data from a fecal egg count reduction test, applying practical modifications to fit the situation on the farm. Which is suitable for all anthelmintics, including ones undergoing metabolism within the host and can be easily applied in goats (Coles, 2005). This test considered to be reliable if more than 25% of the worms are resistance. generally it compares the egg count before and after treatment with anthelmintics, obviously an untreated (control) group of animals should be included, in order to any natural change to egg counts. Which may occur during the test period Once resistant helminths are documented, the species should be determined through larval identification (Papadopoulos, 2008).

2.4.2. Egg Hatch Assays / Larval Development Tests
Eggs from feces are incubated with concentrations of the anthelmintic to be tested and the eggs are allowed to hatch. A dose response curve is generated. The advantage of this test is that a single fecal sample can be tested simultaneously for all available classes of anthelmintics.

2.4.3. Other Tests
Larval development tests, adult development tests, and DNA probes have been described in research settings, but are not commercially available at this time.

2.5. Control of Anthelmintics Resistance
2.5.1. 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. Therefore, strict quarantine procedures should be instituted for all new additions. 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 (Utzinger and Keiser, 2004).

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 anthelminthic therapy, and perform fecal egg count reduction tests. Feed should be withheld for 24 hours before treatment, then 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 anthelminthic 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 (Fleming et al., 2006)

2.5.2. A combination drug strategy

Treating simultaneously with 2 drugs from different anthelminthic classes is one method of preventing the development of anthelmintic resistance (Fleming et al., 2006). A computer based model has documented that if this strategy is used when the drugs are first introduced, before there is any selection for resistance to either drug, appreciable resistance will not develop for over 20 years. However, once resistance alleles accumulate in worm populations, this strategy will probably not be successful. Compared with individual drug effects, anthelmintics of different chemical classes administered together induce a synergistic effect, resulting in clinically relevant increases in the efficacy of treatment. This synergistic effect is most pronounced when the level of resistance is low. Once high level resistance to both drugs is present, the synergistic effect is unlikely to produce acceptable levels of efficacy. In contrast, the same model indicated that rotating drugs with each treatment, using annual rotation or a 5 or 10 year rotation resulted in high level resistance within 15 to 20 years (Van wyk, 2001).

Thus, the common recommendation of annual rotation must be challenged. Rotation of drugs was originally suggested on the basis of the hypothesis that reversion to susceptibility (or at least substantial decrease in resistance gene allele frequency) might occur if resistant worms were less fit than were susceptible worms, and counter selection was applied via treatment with a drug from a distinct chemical class. However, evidence that resistant worms are any less fit or that true reversion occurs in the field is scant. Despite this, the concept of rotation is often viewed as a bona fide resistance prevention scheme, which it is not. Therefore, some leading small ruminant parasitologists are now calling for an end to the practice of rotation (Van wyk, 2001).

It is suggested that a drug should be used until it is no longer effective, then a different drug should be used. For veterinary parasites, a combination of mebendazole and levamisole has been shown to be synergistic against H. contortus in sheep (Radostits et al., 2007).

Generally the development of anthelminthic resistance can be discouraged by changing the class of anthelminthic used for each years; dosing program (Boden, 2005). Do not under dose, use an effective drug in most efficient manner and make sure that the farmer is aware of the problem and consequence of anthelminthic resistance; education is the principal requirement for assisting resource poor farmers to improve the health, productivity and welfare of their animals. Without knowledge, the resource poor farmer cannot improve herd management and prophylaxis of disease by means of vaccination. Knowledge is required to be able to recognize the importance of specific disease conditions and circumstances favoring their development, for instance a greater awareness of the presence and pathogenic effects of nematodes, the epidemiological conditions that are optimal for their survival, and how to manage the infections for the long term. (Radostits et al., 2007).

3. MATERIALS AND METHODS

3.1 Study Area

The study was conducted from January 2018 to July 2018, on goats originated from Arero district of Borana zone. Arero is one of the woredas in the oromia regional of Ethiopia, part of the borea zone, arero is bordered on the southwest by Dire, on the west by yabelo, on the north by Hagere Mariam, on the northeast by the Guji zone, on the east by the Somali region, and on the south by Moyale; the only river in this woreda, separates arero from odo shakiso and Liben. The altitude of this woreda ranges from 750 to 1700 above sea level. Its population are urban dwellers, which is greater than the Zone Average of 11.6%.With an estimated area of 10,841.88 square kilometers, Arero has an
estimated population density of 4.1 people per square kilometer, which is less than the Zone average of 21.1 (CSA 2005).

A survey of the land in this woreda shows that 20% is arable (1.7% was under cultivation), 40.3% pasture, 1.6% forest, the remaining 38.1% is considered swamp, mountainous or otherwise unusable (SPDZ 2006). Arero has 260 kilometers of dry weather roads, for an average road density of 24 kilometers per 1000 square kilometers. About 33.8% of the urban and 12.5% of the rural population has access to drinking water (SPDZ 2006). The 2007 national census reported a total population for this Woreda of 48,126, of whom 24,281 were men and 23,845 were women; 3,004 or 6.24% of its population were urban dwellers. The majority of the inhabitants said they practiced traditional beliefs, with 67.73% of the population reporting they observed these beliefs, while 22.67% of the population were Muslim, 6.82% were Protestant and 2.62% practiced Ethiopian Orthodox Christianity (CSA 2005).

Figure 1: Administrative map of Ethiopia and Borana zone study areas.

Source: Google map

Its pattern is of a bimodal type with 60% occurring in the long rainy season (Gana) extending from mid-March to May and the small rainy season (hagaya) from mid-September to mid-November. The other two seasons are the cool dry season (adolessa) extending from June to August and the major dry season (bona) from December to February (BZDPED, 1998). The districts were selected primarily because the zone is important as a source of animals for domestic consumption and export (Coppock, 1994) and also the districts are the most affected by drought. Animal husbandry in the area is characterized by extensive pastoral productions system and seasonal mobility. Surface water is a serious problem in the area. Traditional deep wells “ellas”, ponds, perennial spring, permanent river (Dawa) and seasonal sources (streams, ephemeral ponds and shallow wells) are water sources for both human and live stocks. Deep wells and large ponds (Machine excavated) are used in dry season while seasonal streams, ephemera ponds and shallow wells are used in wet seasons (Helland, 1982).

3.2. Study of Animal population

The livestock population of the district was estimated Cattle 175000, Goats 110585, Sheeps 49691 (Arero district pastoral Development bureau, 2008).

3.3. Study design and study animals

The screening examination was done from the goats’ population in Arero district that kept in traditional backyard management system with an age range of 6–18 months, and then suitable
arrangements and agreements was made with those farmers who were willing to have their animals used in a faecal egg count reduction test (FECRT). After agreements were made the fecal samples from 384 goats were directly collected from the rectum, the eggs of parasite were counted by using the modified McMaster technique and the result was recorded using the owner’s name with the animal name which given depend on body mark, gift and their behavior, for ease of identification. Goats with more than 150 eggs per gram (EPG) of faces were eligible for inclusion in the field experiment on Anthelmintic resistance; following guidelines by Coles et al. (1992).

Simple random sampling design was employed for this field experimental study (Gomez and Gomez, 1984). For fecal egg count of these 80 goats with fecal egg counts greater than 150 were selected for Anthelmintic resistance study (Coles et al., 1992) the selected goats were randomly assigned in to four groups, each group contain 20 goats: the first group for albendazole, the second group for tetramisole, the third group for ivermectin treatment and the fourth group for control. The faecal sample of each goat under experiment was taken again 11-12 days after treatment, the eggs count was done as previously done pre-treatment in order to compute the variation of eggs number before treatment and after treatment.

The Anthelmintic resistance assessment was conducted from January 2018 to July 2018, on 80 goat’s located Arero district. All goats under experiment treated with different Anthelmintic according to the manufacturer’s recommended dose rate except control group. Fecal samples were directly collected from rectum again 11 to 12 days post-treatment from all goats under study, the nematode faecal egg counts were made by using the modified McMaster technique (Coles et al., 1992).

<table>
<thead>
<tr>
<th>Table 1: Table of drug used and their route of administration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Trade name</strong></td>
</tr>
<tr>
<td>Albenda</td>
</tr>
<tr>
<td>Ashiteta</td>
</tr>
<tr>
<td>Noromectin</td>
</tr>
</tbody>
</table>

The Anthelmintic resistance was evaluated on the basis of the reduction in faecal egg count. Calculation of the Anthelmintic mean, percentage reduction and 95% upper and lower confidence limits was according to Coles et al. (1992). Resistance is declared if the percentage reduction was less than 95% and the 95% lower confidence limit is less than 90%. Hence the interpretation of result was given based on this guides.

4. RESEARCH RESULT

The faecal samples collected from 384 goats during the screening indicated that 201(52.3%) of the studied goats were shedding gastrointestinal nematodes eggs in their faeces (Table 2). The mean egg count per gram of faeces was 684.55 ± 119.7.

<table>
<thead>
<tr>
<th>Table 2: Prevalence of goats’ gastrointestinal nematodes in Arero district</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Factor</strong></td>
</tr>
<tr>
<td>Sex</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Overall</td>
</tr>
</tbody>
</table>
Table 3: Summary of mean gastrointestinal egg count per gram of faeces

<table>
<thead>
<tr>
<th>Species</th>
<th>Category</th>
<th>No of animals examined</th>
<th>Mean EPF ± Std. Error</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Male</td>
<td>169</td>
<td>311.79 ± 29.96</td>
<td>258.99 378.08</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>215</td>
<td>372.76 ± 31.25</td>
<td>310.83 434.70</td>
</tr>
<tr>
<td>Age</td>
<td>Young</td>
<td>214</td>
<td>331.09 ± 29.58</td>
<td>272.50 389.67</td>
</tr>
<tr>
<td></td>
<td>Adult</td>
<td>170</td>
<td>374.39 ± 32.32</td>
<td>310.06 438.71</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td>384</td>
<td>684.55 ± 61.9</td>
<td></td>
</tr>
</tbody>
</table>

The mean pre and post treatment faecal egg counts (EPG) and the percentage of faecal egg count reduction (FECR) and the lower and upper 95% confidence limit for each groups of anthelmintic drugs tested was summarized in Table 4. The percentage reduction of faecal egg count, (95% confidence intervals) for albendazole, ivermectin and tetramisole were 87.2% (470.30 to 703.69), 81.06% (431.10 to 598.89) and 96.15% (506.47 to 658.52) respectively. Among the three drugs, tetramisole are a faecal egg count reduction percentage above 95%, and other is less than 95% percentage. Hence result indicated that albendazole and ivermectin were suspected for development of resistance against gastrointestinal nematodes, while tetramisole was found to be effective.

Table 4: Table to show the results of pre-treatment and post-treatment faecal egg count and reduction percentage in goats at Arero

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>EPG</th>
<th>Reduction %</th>
<th>95% CL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-treatment</td>
<td>Post-treatment</td>
<td></td>
</tr>
<tr>
<td>Albendazole</td>
<td>695 ± 49.504</td>
<td>108 ± 16.56</td>
<td>87.2% (470.30 - 703.69)</td>
</tr>
<tr>
<td>Ivermectin</td>
<td>675 ± 42.68</td>
<td>160 ± 21.94</td>
<td>81.06% (431.10 - 598.89)</td>
</tr>
<tr>
<td>Tetramisole</td>
<td>615 ± 33.26</td>
<td>32.5 ± 6.56</td>
<td>96.15% (506.47 - 658.52)</td>
</tr>
<tr>
<td>Control</td>
<td>682.5 ± 40.761</td>
<td>845 ± 65.68</td>
<td>-</td>
</tr>
</tbody>
</table>

5. DISCUSSION

The coprological examination performed for this study using direct faecal floatation method revealed the existence of gastrointestinal nematodes with an overall prevalence rate of 52.3% in the goat examined. The current prevalence was slightly lower when compared to various research outputs in Ethiopia by, Tefera et al. (2011) in and around Bedelle, Moti (2008): In and around Welinchity, Tesfaheywet (2012) in and around haramaya and who reported 93.29%,76.3% and 61.4%, respectively. The higher prevalence observed in different parts of Ethiopia could be ascribed to over stocking, poor nutrition (starvation), poor management practice of the animals (lack of sanitation) and frequent exposure to the communal grazing lands that have been contaminated. However, the finding is higher than previous studies reported 40.6% by Biqila et al. (2013) from Gechi District, Southwest Ethiopia.

From a total 384 goats examine during the screening 201(52.3%) of the goats were found infected with gastrointestinal nematodes in Arero district. There was no significant variation in the infection of age and sex groups ($\chi^2 = 2.064, P = 0.91$; and $\chi^2 = 0.012$ and $P = 0.497$, respectively). The anthelmintics resistance was evaluated depend on arithmetic mean, percentage reduction and 95% upper and lower confidence limit were computed using the guide and formula described by Coles et al (1992).

Depend on this formula the FECR% of ivermectin group, albendazole group and tetramisole group were 81.06%, 87.2% and 96.15% respectively. Based on this criterion, the FECR percentage and the lower confidence limit obtained from Arero district smallholder goats production system revealed the presence of a significant level of gastrointestinal resistance to albendazole and ivermectin. This finding is disagree with other studies conducted in various parts of Ethiopia, on the efficacy of the most commonly used anthelmintics in small ruminants (Asmare et al., 2005; Kumsa and Abebe, 2008; Kumsa and Nurfeta, 2008; Kumsa and Wossene, 2006; Sheferaw and Asha, 2010; Tadesse et al., 2009;
Sheferaw et al., 2013). However it agrees with albendazole resistance with Sheferaw et al., 2013; Bersisa and Girma, (2009) reported except on tetramisole and absence of resistance of tetramisole with this study. Furthermore this finding was total disagree with Asmare et al. (2005) who reported ivermectin and albendazole susceptibility and resistance for tetramisole.

Mostly believed that benzimidazoles are the most widely used anthelmintic family followed by the macrocyclic lactone in the study area. It also indicated that the imidazothiazoles family is used only by institutional farms who keep animals under intensive management system. It also revealed that farmers in the study area perform several practices that may be responsible in lowering the efficacy of anthelmintics that agrees with many earlier studies conducted elsewhere in the world (Arece et al., 2004; Chandrawathani et al., 2004). Studies on efficacy of anthelmintic drugs are useful to establish and maintain effective and sustainable control strategic against helminthes of livestock, especially for small ruminants.

Efficacy evaluations of the anthelmintics carried out and interpreted as per the WAAVP recommendations provided evidence of susceptibility of nematodes to tetramisol families. This finding agree with previous studies conducted on small ruminants maintained under extensive type of production by resource poor smallholders in some parts of Ethiopia (Kumsa and Wossene, 2006b; Sissay et al., 2006a,b) and with other studies in different parts of the world (Arece et al., 2004; Saddiqi et al., 2006).

The lower efficacy of ivermectin and albendazole against nematodes of goats in this study area might be caused several factors like poor quality drugs of low price, continuous under dosages treatments at the drug dose rate by pastoralists due to low bioavailability in goats, misuse smuggle drug and inappropriate treatment by owners. Similar factors have already been reported to contribute to lower efficacy (Chandrawethani et al., 2004; Saddiqi et al., 2006; Saeed et al., 2007).

6. CONCLUSION
From this study, we can conclude that albendazole and ivermectin is not effective in the area against gastrointestinal parasites. Gastrointestinal nematodes in Arero, were suspected for development of resistance against albendazole and ivermectin, while tetramisole was found to be effective. On the other hand, both albendazole and ivermectin showed lower efficacy, especially against nematodes in goats of the study area. However, many factors like use of drugs from black market, under dosage, misuse and inappropriate treatments may all hasten failure in efficacy of currently efficacious anthelmintics.

Depending on the above fact the following recommendations were forwarded

➢ As a result to maintain and prolong, the lifespan of the efficacy of available drugs pastoralist should be educated by proper veterinary extension about the importance of correct use of anthelmintics, annual rotations anthelmintic group and avoiding all factors that favor reduction in efficacy leading to anthelmintic resistance.

➢ Further studies should be conducted based on a comparative efficacy of drugs from reliable source and drugs used by the owners from unreliable sources such as imported drugs or smuggle drugs.

➢ Furthermore to prevent development of anthelmintic resistance in this area, the following practices will be helpful: avoid frequent and unnecessary treatments with anthelmintics and avoid under dosing of animals.

7. ACKNOWLEDGEMENTS
All the praises and thanks be to Allah for his favour to me in completing my work and without whom I would have not been successful.

Next, I would like to express my grateful thanks to my advisor Dr. Fatu Mudasir and my co advisor Dr. Gobu Boru for their intellectual guidance, helpful input, valuable comment and devotion of time in preparing this research. Furthermore I would like to thank my family, all teachers/instructors who provide their input to reach here specially Dr Belay Abebe, my classmates and other students who give constructive idea. I wish to extend my heartfelt thanks to staff of Adami Tulu Agricultural Animal Health Laboratory, for support of laboratory materials, reagents and for their assistance and

Zambrut.com
Abduljami, G. Anthelmintics Resistance on Goat Gastrointestinal..............
encouragement. Besides I would like to thank animal health laboratory team for their material support and moral encouragement during the period of my research work.

8. REFERENCES

54. Socio-economic profile of the Borena Zone Government Oromia Region (last accessed1 August 2006)
8. ANNEXES

Annex 1. Description of dentition with corresponding age estimates protocol

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Age (in months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young with fully grown milk teeth</td>
<td>9</td>
</tr>
<tr>
<td>The milk teeth started to wear down, or are fully spread out</td>
<td>12</td>
</tr>
<tr>
<td>With erupted &amp; growing 1st pair of permanent teeth</td>
<td>14 – 17</td>
</tr>
<tr>
<td>With erupted &amp; growing 2nd pair of permanent teeth</td>
<td>18 – 23</td>
</tr>
<tr>
<td>With erupted &amp; growing 3rd pair of permanent teeth</td>
<td>24 – 36</td>
</tr>
<tr>
<td>With erupted &amp; growing 4th pair of permanent teeth</td>
<td>3 – 5</td>
</tr>
<tr>
<td>The four pair of permanent incisors have started to Wear down</td>
<td>4 years</td>
</tr>
<tr>
<td>The permanent incisors have worn down &amp; have started to spread out</td>
<td>&gt;5 years</td>
</tr>
</tbody>
</table>

Source: (Yami and Merkel, 2009)

Annex 2. Sample collection format

<table>
<thead>
<tr>
<th>ID</th>
<th>Spp</th>
<th>Sex</th>
<th>Age</th>
<th>Origin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Annex 3. McMaster Egg count

McMaster Egg count is quantitative method for determining the number of nematode eggs per gram of feces in order to estimate the worm burden in an animal. The advantage of this method is it is quick as the eggs are floated free of debris before counting, the disadvantage is you must use a special counting chamber.

1. 4 grams of feces was taken and grinded.
2. The mixture of feces and floatation solution was passed through sieves. Lift the sieve and hold over the dish. Push out any remaining solution from the feces.
3. While mixing vigorously (you may want to put the solution into a flask to prevent spillage) take a sample of the mixture with a pipette and transfer it to one of the chambers of the McMaster slide. Repeat the procedure and fill the other chamber.
4. Wait 30 sec then count the total number of eggs under both of the etched areas on the slide. Focus first on the etched lines of the grid, then go down a tiny bit, the eggs will be floating just below the top of the chamber. Multiply the total number of eggs in the 2 chambers by 50; this is the eggs per gram (EPG).