

Alternative Control Methods of Gastrointestinal Nematode Infections in Small Ruminants: Biological Method and Use of Medicinal Plant Extracts

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Abstract: Diseases caused by gastrointestinal nematodes (GINs) in livestock are a major production constraint, causing economic losses, especially in small ruminants in the tropics and subtropics. The infection of sheep and goats by nematodes is rampant in most African countries, where the environmental conditions are conducive to nematode growth and transmission. In general, GINs reduce productivity of small ruminants due to lowering fertility, reduction in milk production and loss of weight when feed intake is reduced. Currently, the conventional control strategy for GIN infections is the use of synthetic anthelmintic drugs. However, several problems associated with the use of these anthelmintics have been observed worldwide. Among these problems, development of drug resistance to the available drugs is widespread. Development of resistance has been attributed to the extensive therapeutic use of anthelmintics. Consequently an alternative control measures are much needed. Medicinal plants may become good alternatives for modern synthetic anthelmintics if their efficacy is proved scientifically under controlled studies. Plant-based drugs are believed to be less toxic to the host and end-users, easily available, biodegradable, cheaper and eco-friendly. Several families of plants such as the Lamiaceae, Caesalpiniaceae and Meliaceae are being investigated for their efficacy against various helminth parasites. Methodologies used for treating animals with plant materials includes the provision of fresh, conserved or dried plants, the use of crude aqueous and solvent extracts and administration of fractionated materials from the crude products. In addition to herbal medicines, biological agents have shown positive results in controlling GINs such as fungus *Duddingtonia flagrans* and bacterium *Bacillus thuringiensis*. The objective of this review is therefore to highlight some advances in the study of herbal medications and biocontrolling agents including the methodology as well as outlines future research fields.

Keywords: Anthelmintics, Biological control, Helminthes, livestock, medicinal plants, nematodes

1. INTRODUCTION

Infections by gastrointestinal helminth parasites of livestock are among the most common and economically important diseases of grazing livestock. They are characterized by lowering outputs of animal products (meat, milk, hides and skins), manure and traction (Perry *et al.*, 2002). In the Developed world, with the exception of those countries in the southern hemisphere, the greatest impact is probably the costs of control, particularly in the case of the helminth parasitoses. In the Developing world, the greatest impact of parasitic diseases is attributed to the potential productivity losses. In addition, there are highly pathogenic nematode (*Haemonchus spp.*), and trematode (*Fasciola*

spp.) of ruminants which are also capable of causing acute disease and high mortality (Githiori, 2004). *Haemonchus contortus* is one of the top 10 constraints of sheep and goat production in East Africa.

The current methods of gastrointestinal nematode (GIN) control are based on repeated use of synthetic anthelmintic drugs (such as Benzimidazoles, Imidazothiazoles and macrocyclic lactones). However, with increasing exposure by routine dosage of small ruminants, GIN are developing resistance to most commercial anthelmintic drugs (Coffey *et al.*, 2007). Resistance to anthelmintics is demonstrated by the ability of GIN to survive drug treatments that used to be effective against

the same species and stage of infection (Coffey *et al.*, 2007). Secondly, consumers of animal products have also become cautious of possible contamination of meat and milk products by residues of drugs. At the other end, small-scale farmers are being pushed out of the small ruminant farming by GIN due to their inability to treat them effectively because of the high price of effective drugs. There is a need to rethink the use of anthelmintics, as well as develop novel approaches, which will lead to sustainable control of parasites. Ideally, this may entail an integrated approach, including reduced frequency of anthelmintic treatments, biological control, parasite vaccines, livestock breeds that are resistant to parasites and the use of plants with anti-parasitic properties (Waller, 2003).

Biological control is becoming an important non-chemical option for controlling GIN in animals since biocontrol agents can control a target organism by reducing its population to a level that no longer causes clinical problems and economic losses. In addition, biocontrol agents have low mammalian toxicity, high efficacy, naturally occurring and multiply to a level that matches its target organisms (Larsen, 2006). Thus, biocontrol agents can avoid the issue of chemical residues in food and is an attractive option for organic farming. However, there are no commercial biocontrol agents currently available for controlling GIN in livestock anywhere in the world.

Traditional medicines hold a great promise as sources of easily available effective anthelmintic agents (Temjenmongla and Arum, 2005). Most of these plants are readily available in the tropical and sub-tropical region that may be affordable to all farmers including smallholder farmers (Akhtar and Malik, 2000). In ethnoveterinary medicines, which draw inspiration from traditional practice, there seems to be a range of plants or plant extract suitable for treating almost every parasitic disease of livestock (Athanasaidou *et al.*, 2007). Research for biocontrolling agents and traditional medicinal plants in treatment of parasitic gastrointestinal nematodes is still in progress.

The objective of this seminar paper is therefore to highlight current knowledge on the research and application of medicinal plant extracts and biocontrol agents as alternative medication to

modern chemotherapy against GI nematode parasites of small ruminants.

2. GASTROINTESTINAL NEMATODE

2.1. The Parasites and Their Epidemiology

Gastrointestinal nematodes are the most damaging parasites in small ruminants (Abuda *et al.*, 2010). In Africa, particularly, the infection in most cases is by members of the class nematoda. The major ones include: *Haemonchus contortus*, *Trichostrongylus colubriformis*, *Bunostomum trigonocephalum* and *Oesophagostomum* spp. Most of these parasite species have been reported from different areas of Africa including Ethiopia (Waller, 1997). Animals raised in confinement or on pasture-based systems will almost certainly be exposed to gastrointestinal parasite at some point in their lives (Min and Hart, 2003). All types of livestock are at risk to gastrointestinal nematode infection which varies in their host range, life cycle and severity. However, small stock is the most susceptible to gastrointestinal nematode infections (Tsotetsi & Mbatia, 2003).

The nematode life cycle (Figure 1) may be direct or may include an intermediate host. Sexes are usually separated (male and female). However, the economically important gastrointestinal parasites (Strongylid) in sheep and goats have direct life cycles, with no intermediate host (Sissay, 2007). Mature parasites (worms) breed inside the host and lay eggs which are shed in faeces. After eggs pass out of the host, they hatch into first-stage larvae (L1), which grow then moult into second-stage larvae (L2) under appropriate conditions of temperature and humidity. Larvae need moisture to develop and move. During this time, larvae (L2) feed on bacteria, and then moult into infective larvae (L3), which migrate out of faeces and climb up blades of grass. The time for development from egg to infective larvae can be as short as 7-10 days, especially during summer. Further, when an animal (sheep or goat) grazes, it may ingest parasitic larvae along with the grass. Normally the L3 stage larvae moult into fourth-stage larvae (L4) within 2-3 days, then after a further 10-14 days, they moult into young adult parasites (Hale, 2006; Coffey *et al.*, 2007). The time from ingestion of infective larvae to adult laying eggs, called the pre-patent period, vary among nematode.

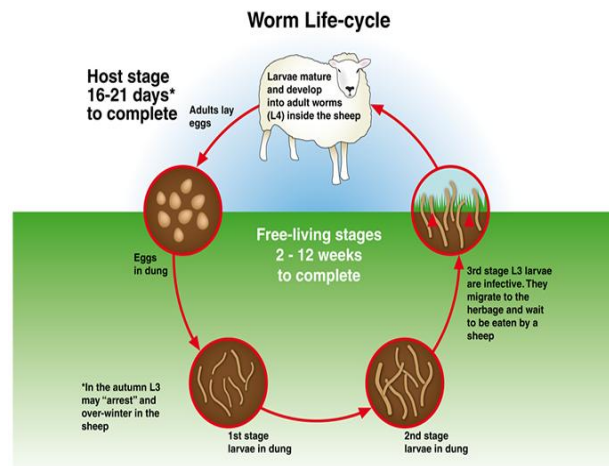


Figure1. Life cycle of gastrointestinal nematodes of small ruminants. (Scheuerle, 2009).

The development, survival and transmission of the free-living stages of nematode parasites are influenced by micro-climatic factors within the faecal pellets and herbage. These include sunlight, temperature, rainfall, humidity and soil moisture. Under optimal conditions (high humidity and warm temperature), the development process takes 7 to 10 days, but for *H. contortus* a more rapid translation of eggs to larvae can occur in warm wet conditions. Infective stage of nematode can survive for weeks to months on the pasture depending on the weather conditions and the nematode species (Stromberg and Averbek, 1999).

2.2. Pathological Impact and Diagnosis

Nematodes usually live in the digestive system of host animals, affecting the absorption and/or retention of minerals especially phosphorus (Coop and Kyriazakis, 2001). Effects of nematodes on the host include loss of condition, rough coat, diarrhoea, bottle jaw, anaemia and death (Hale, 2006). Moreover, clinical signs such as diarrhoea, weight loss and loss of appetite can be indicators of nematode infection, especially in young animals (Sissay, 2007). Livestock nematodes have economic consequences when their numbers rise under suitable conditions (Hale, 2006).

Parasitism by nematodes results in the loss of host protein like plasma and frequently erythrocytes exfoliated epithelial cells and mucus. A Pale to grayish colouring of mucus membranes like eye lids, gums, and vulva, can be seen due to lack of red blood cells. Nematode parasites also affect digestion, energy and nitrogen utilization in the parasitized animal and reduce the performance of the host and feed consumption (Simcock *et al.*, 2006).

Diagnoses of nematode infection in the host can be done by examination of the host faeces for parasitic eggs and larvae (Knox and Faedo, 2001). Demonstration of parasite eggs or larvae in the faeces or faecal culture provides evidence that the host is infected, but does not indicate the level of infection (Hansen and Perry, 1994). Heavy nematode infection is indicated by finding more than a thousand eggs per gram (EPG) of faeces. Between 200 and 800 EPG of faeces would count as a moderate nematode infection. However, the level of infection from faecal egg or larvae counts is variable in each country or region, according to weather conditions and the nematode's specific pathogenicity (Lindqvist *et al.*, 2001).

2.3. Economic Importance of Parasitic Gastrointestinal Nematodes

Parasitic gastrointestinal nematode infections are of major economic importance resulting in heavy production losses in small ruminants than cattle. According to Egualé *et al.* (2007), gastrointestinal nematode infections accounts for 28% mortality and 8% of weight loss in sheep mostly in developing countries with poor socio economic status and poor management practices. Infected animals produce less quality of wool, meat and milk due to the observed clinical symptoms (Iqbal *et al.* 2010). Rate of production is also hampered because reproduction performances of infected animals are affected (Nchu *et al.* 2011).

Losses due to GIN parasitism estimated by governmental organizations extend into millions of dollars per year, but it is difficult to assess these losses because there are many factors involved. Such factors and their interaction include nutrition, environmental stress, genetics,

management and concurrent disease. For example, in New Zealand, it was estimated that NZ\$200 million of production annually was still not being realized after taking into account the cost of nematode parasite control (Vlassov *et al.*, 2001); in Australia, with increasing anthelmintic resistance, estimated losses were up to AD\$700 million annually (Besier and Love, 2003); and Ethiopian meat markets and the export of livestock have an estimated annual loss of US\$400 million (Kumsa, 2006).

2.4. Major Control Methods

2.4.1. anthelmintics

Anthelmintic drugs are chemotherapeutic agents commonly used either for prophylactic purposes, in which the timing of treatment is based on a knowledge of the epidemiology, or for therapeutic purposes to treat existing infections or clinical outbreaks. Various groups of drugs such as Piperazine (ex. Piperazine salts), Benzimidazoles (ex. Albendazole), Salicylanilides (ex. Closantel), Macrocyclic lactones (ex. Ivermectin) and Imidazothiazoles (ex. Tetramisole) have been shown to be successful (almost 100%) in eliminating most species of nematodes and trematodes during their early periods of utilisation, and some still remain effective in different parts of the world (Getachew *et al.*, 2007). However, there are several evidences to show that resistance has already been developed or emerging against most of the anthelmintic groups by many species of nematodes (Chartier *et al.*, 2001). Their long term utilization, inappropriate handling and under dosage may be some of the reasons for their reduced efficacy and for the increasing development of drug resistance. Development of anthelmintic resistance begins with the loss of efficacy of the drug on the nematodes which on later stages renders the expensive drug useless (Roeber *et al.* 2013).

Anthelmintic resistance is a threat to agricultural incomes because parasitic gastrointestinal infection rates only escalate and as a result heavy production losses will remain a major problem to livestock (Wolstenholme, 2004).

Benzimidazole, imidazothiazole and ivermectin all leave residues in meat, milk and their products. On the other hand, ivermectin is excreted in faeces in sufficient quantity to have a detrimental effect on invertebrates that usually degrade dung heaps, and hence on organisms higher up the food chain (De and Sanyal, 2009).

Moreover, where these drugs are not easily accessible either because of economic reasons or scarcity of veterinary services, as in most parts of Africa, animals die as a result of acute disease. These altogether urgently calls up on effective alternative or complementary methods of control.

2.4.2. Alternative Control Methods

Because of the above and other limiting factors, other means of gastro-intestinal nematode control have been explored such as using copper wire particles, grazing management, breeding for host resistance, vaccination, using plants extracts and biological control. Copper wire particles, Grazing management, breeding for host resistance, vaccination strategy, nutrition, biological control and use of medicinal plant extracts have been tried with varying success (Soli *et al.*, 2010; Mitreva *et al.*, 2007).

3. BIOLOGICAL CONTROL AND USE OF MEDICINAL PLANT EXTRACTS

3.1. Biological Control

3.1.1. Concept of biological control

In general, biological control of nematodes becomes an important, integrated element and sustainable strategies to control nematodes in livestock Biological control defined as the activity of natural enemies which include classical, un-exploited organisms and genetically modified organisms (Larsen, 2006).

Biological control might be different from other methods which are directed at the parasitic stages within the host. However, biological control is targeted at the free-living stages on pasture (Waller, 2006). This means that biological control focuses on the faecal deposits in which eggs, L1, L2 and L3 larval stages are found. The entire philosophy of using biological control agent against GIN nematodes in animals is to reduce the number of infective stages that are available to be picked up by grazing susceptible individuals of the different species of livestock (Waller, 2006). Biological control of nematodes in livestock aims to establish a condition where grazing animals are exposed to a low number of infective larvae and reduce the level of nematode parasitism in livestock so that natural immunity in the animals will tolerate these low levels (Epe *et al.*, 2009). An important issue is that biocontrol agents have no negative effects on the environment. However the effect on animals requires investigation. Furthermore, biocontrol agents are free of chemicals, thus

producers can capitalize on the residue-free, organic meat products that are in high demand from consumers and command a premium price (Waller, 2006).

Therefore, for the near future, the greatest research effort in the quest for biological control agents of animal nematode parasites is likely to be focused on those organisms in the external or free living, environment. This is because a large range of organisms can exert their effects indirectly, by habitat (dung) destruction, or directly by using the free living stages as a food source. Others have been suggested as potential candidates, such as earthworms, viruses, soil amoeba, protozoa, collembolans, mites, fungi, nematodes itself and bacteria (Thamsborg *et al.*, 1999).

3.1.2. Earthworms

Earthworms are a vital component of the soil ecosystem. Earthworm populations consume large volumes of soil and organic matter, including animal faeces (Grønbold *et al.*, 1996). During feeding, they consume nematodes present in soil and faeces. Earthworm actively participate in the destruction of eggs and larvae by digesting them or transferring them to deeper levels of the soil where chances that they can reach the surface as infective larvae are very low (Grønbold *et al.*, 1996). However, these earthworms are only active in moist habitats, which limit their biological control potential. They may reduce transmission by degrading faecal pats but they may also prolog the survival of larvae by taking them into the soil.

3.1.3. Dung Beetles

The term 'dung beetle' refers to those beetles that live partly or exclusively on the dung of herbivorous; most species belong to the family *Scarabaeidae*. Adult beetles use the liquid contents of manure for their nourishment and some species form dung balls which they bury and lay their eggs in, others just live in the manure pats (Thomas, 2001). The activity of dung beetles is being discussed controversially: by breaking up the pats and partially burying the manure, they enhance the drying up of the dung which deteriorates growing conditions for larvae (Grønbold *et al.*, 1996) but by the same activities in bad weather conditions they might help the larvae to survive by airing out the pats and thereby providing oxygen to the larvae (Vlassoff *et al.* 2001).

3.1.4. Viruses

Cases of livestock nematodes infected by nematopathogenic viruses have been reported (Stiffling, 1991). One challenge is that it is difficult to recognize viral infection in microscopic nematodes, or differentiate sick nematodes from those that are diseased or immobile for some other reason (Waller and Faedo, 1996). Consequently, viral pathogens against free living stages of animal parasitic nematodes are unlikely to be developed as commercial products.

3.1.5. The soil amoeba, *Theratomyxa weberi* Zwillenberg

Theratomyxa weberi Zwillenberg can trap the nematode and digests it within a day. However, Grønbold *et al.* (1996) indicated that *T. weberi* and other amoebae have limited biological control capacity because they are slow-moving compared with nematodes, and they are sensitive to low soil water potentials, conditions under which nematodes may survive.

3.1.6. Protozoa

Protozoa have been used as biological control agents for nematodes and for insects control (Lacey *et al.*, 2001). Most promising species seem to be those that produce spores which attack nematodes following ingestion. However, this ingestion is prevented in many nematode species by the narrow bore of their style canal (Waller and Faedo, 1996). For this reason, protozoa might not offer a high class opportunity for biological control of nematode parasites of livestock.

3.1.7. Micro-arthropods

A number of soil invertebrates have been tested for their potential as biological control of nematode parasites. Micro-arthropods such as collembolans and mites may be effective options. The mechanisms by which collembolans and mites affect nematodes have not yet been determined. Collembolans and mites are capable of consuming *Ascaris suum* eggs (Akhtar and Malik, 2000).

3.1.8. The fungus *Duddingtonia flagrans* Cooke

Use of nematophagous fungi may be a way to reduce pasture contamination and parasite populations. A number of fungal species have shown anthelmintic properties (Epe *et al.*, 2009). These fungi are able to attract and kill the

developing larval stages of parasitic nematodes in a faecal environment (Table 1.5), either as a primary source of nutrients or as a supplement to a saprophytic existence (Waller *et al.*, 2006). According to their morphology, functional characteristics and the way they capture nematode parasites, these fungi are divided into three main classes: predacious, endo-parasitic and egg-destroying fungi (Waller and Faedo, 1996). The fungus *Duddingtonia flagrans* is one of the fungi that traps nematodes and has shown much promise as a biological agent. This fungus belongs to a heterogeneous group of fungi in the Deuteromycetes family (Waller *et al.*, 2006). Specifically, *D. flagrans* is a predacious fungus that produces adhesive three dimensional hyphal networks during development, which trap the larval stages of nematodes (Campos *et al.*, 2008).

This fungus has shown its ability to survive through the digestive system of ruminants as a resistant spore (chlamyospore) form (Manueli *et al.*, 1999) and has demonstrated its potential to consistently and significantly reduce the numbers of infective *Trichostrongyle* larvae and most of the economically important gastrointestinal parasites, when applied in animals feed as fungal spores (Larsen, 1999). Knox and Faedo (2001) reported a reduction in nematode larvae count and an improvement in live weight gains in sheep fed a supplement containing *D. flagrans* chlamyospores compared to untreated sheep.

The dosage of *D. flagrans* spores which affect nematode parasites negatively has been reported in many studies. For example, a fungal dose of 5g of grain/sheep per day for 2 consecutive days reduced larval numbers in faecal culture in an *in vitro* study (Waller *et al.*, 2001). In addition, Larsen *et al.* (1998) demonstrated that sheep fed a dose of 5×10^5 *D. flagrans* chlamyospores per day resulted in a substantial (more than 80%) reduction in the number of infective larvae derived from nematode eggs in faeces. Moreover, dosing calves with 106 *D. flagrans* chlamyospores per kg BW daily was sufficient to significantly reduce herbage infectivity and subsequently infection levels (Sarkunas *et al.*, 2000). Another study in the equine field reported that dosage of 2×10^6 chlamyospores per kg BW were effective in reducing numbers and transmission of equine nematode L3 stages from faecal pats to surrounding herbage (Baudena *et al.*, 2000). More importantly, feeding of daily dosages of 2.5×10^4 to 5×10^5

D. flagrans chlamyospores per kg BW can control larval stages of *H. contortus* in sheep (Peña *et al.*, 2002).

Duddingtonia flagrans traps the free-living larval stages, which include eggs, L1 and L2 stages within the faecal deposit, and infective third-stage larvae on pastures. *D. flagrans* can survive passage through the gastrointestinal tract in the host and might be effective in trapping larvae present in faeces, thereby reducing pasture larval population. Consequently, chlamyospores are administered orally and deposited in faeces (Faedo *et al.* 1998).

3.1.8. The fungus *Clonostachys rosea f. rosea* Schroers

The fungus is also known as *Gliocladium roseum* Bain which belongs to the family *Bionectriaceae*, and the Order *Hypocreales*. It is widely distributed, facultative saprophyte in the soil. *Clonostachys rosea f. rosea* is a predacious fungus has a potential to control nematodes of plants and animals (Zhang *et al.*, 2008). The fungus has shown its ability to survive through the digestive system of ruminants as chlamyospore form (Baloyi *et al.*, 2012). The fungus also is able to attack many organisms, including other fungi, bacteria, insects and nematode parasites because it produces a wide range of volatile organic compounds. For example, *C. rosea* protects plants against *Botrytis cinerea* by suppressing spore production (Li *et al.*, 2004). Its hyphae grow inside the conidia of *Botrytis cinerea*. In addition, a strain of *C. rosea*, IK726, isolated from barley roots infected with *Fusarium culmorum* was evaluated for its biological activity. The strain IK726 was found to be effective against seed-borne diseases of cereals under field conditions. Moreover, IK726 strain of *C. rosea* controlled *Alternaria radicina* Meier, Drechsler and Eddy on carrot seeds (Jensen *et al.* 2000).

The mode of action of *C. rosea* as biological control agent is not well understood. However, mycoparasitism, substrate competition, enzymatic activity and induced resistance are all thought to play a role (Lübeck *et al.*, 2002). Production of secondary metabolites might provide antibiotic effect as is known for other biocontrol fungi (Roberti *et al.*, 2008). *Clonostachys rosea f. rosea* conidia attach to the cuticle of nematodes, germinate and produce germ tubes, which then penetrate the host body, and kill the nematode (Zhang *et al.*, 2008).

Clonostachys rosea f. rosea produces cell wall-degrading enzymes, including chitin, glucan, and cellulose-degrading enzymes (Roberti *et al.*, 2008). The enzymatic hydrolysis of chitin is catalysed by the action of three types of chitin-

hydrolysing enzymes belonging to glycosyl hydrolase families. These enzymes digest the cell walls of ascomycetes and basidiomycetes, as well as insect skeletons (Mamarabadi *et al.*, 2009).

Table2. Fungal species used to control nematode parasites

Fungal species		Susceptible nematodes
Endoparasitic fungi	Drechmeria	Heamoncus species and trichostrongylus colubriformis
	Harposporium anguillucal	
Predacious fungi,	Arthrobotry soligospora	Ostertagia species Dictyocalus villilpar Heamoncus contortus Oesophagostumum species Cooperia Species
	Arthrobotry misinformis	
	Arthrobotry robusta	
	Monacrosporium endermatum	
Egg parasitic fungi Vertisillium chlamydosporium		Ascaris suum

Source: Larsen, 2000

3.1.9. The bacterium *Bacillus thuringiensis* Berliner

Bacillus thuringiensis Berliner is a gram positive bacterium, found in various ecological niches such as soil, plant surfaces and dust from stored-products (Maagd *et al.*, 2003). *Bacillus thuringiensis* is closely related to *Bacillus cereus* Frankland and Frankland, a soil bacterium, and *Bacillus anthracis* Koch, the cause of anthrax. The three organisms are mainly different in their plasmids (Helgason *et al.*, 2000). Like other members of the genus, all three are aerobes capable of producing endospores.

Bacillus thuringiensis produces crystals of proteinaceous insecticidal δ -endotoxins (crystal proteins or Cry proteins) (Ito *et al.*, 2006). Cry toxins have specific toxin effects against insect species of the orders *Lepidoptera*, *Diptera*, *Coleoptera*, *Hymenoptera*, *Homoptera*, *Orthoptera*, and *Mallophaga* as well as other organisms such as nematodes, mites and protozoa (Maagd *et al.*, 2003). *Bacillus thuringiensis* has received considerable attention because of its utility for control of insect pests in agriculture and insect vectors of human diseases (Maagd *et al.*, 2003; Quesada-Moraga *et al.*, 2004). Basically, *B. thuringiensis* strains have been used to control insect pests since the 1920s (Wood, 2002). *Bacillus thuringiensis* is considered safe to people and non-target species, such as wildlife. Its formulations can be used on all food crops, making it relatively easy to exploit commercially. Moreover, *B.*

thuringiensis does not have dominant alleles, which could be easy to influence genetically (Raymond *et al.*, 2010). Some *B. thuringiensis* strains can kill nematodes (Larsen, 1999). In addition, many *B. thuringiensis* isolates have been found to be highly toxic to larval stages and adults of *H. contortus*, *T. colubriformis* and *O. circumcincta* *in vitro* (Kotze *et al.*, 2005). These studies indicated that *B. thuringiensis* is toxic to both larval stages and adults of economically significant nematodes (Table1.3). Therefore, *B. thuringiensis* strains could be utilized as anthelmintics to kill nematodes of the gastrointestinal tract, and/or the free-living larval stages that develop in faeces or on pastures.

Research on using *B. thuringiensis* to control the free-living larval stages of nematodes resulted in a significant reduction of existing parasites (Kotze *et al.*, 2005). On the other hand, *B. thuringiensis* spores are slow to germinate and develop crystal toxins to disturb the nematode growth (Grady *et al.*, 2007). Notably freshly hatched larvae are more susceptible to *B. thuringiensis* toxins than older ones. These constraints limit the ability of *B. thuringiensis* isolates to inhibit nematode populations (Grady *et al.*, 2007). Wei *et al.* (2003) reported that *B. thuringiensis* uses the same mode of action to kill nematodes. Kotze *et al.* (2005) have shown that different Cry proteins have variable toxicity towards nematodes. For example, *Cry5B* endotoxin kills *Caenorhabditis elegans* (Marroquin *et al.*, 2000). Some protoxins

Cry5B, *Cry6A*, *Cry14A* and *Cry21A* are toxic to a number of free-living stages of nematodes, and *Cry5B*, *Cry14A* and *Cry21A* were highly toxic to the free-living larval stages of the

rodent-parasitic nematode, *Nippostrongylus brasiliensis* (Wei *et al.*, 2003). These studies have confirmed that *Cry* proteins cause damage to the intestine of both nematodes and insects.

Table3. *Effect of biological control agents on nematodes*

Biocontrol agent	Experimental model	Effect on				Reference
		EPG	LPG	WT	L3*	
<i>Arthobotrys dactyloides</i>	Goats and Sheep		+			Sandecris <i>et al.</i> , 2008
<i>Arthobotrys oligospora</i>	Cattle		+			Gronvold <i>et al.</i> , 1985
<i>Catenaria anguillula</i>	Goats and Sheep		+			Sandecris <i>et al.</i> , 2008
<i>Clonostachys Rosea</i>	Sheep	None	+	None		Baloyi <i>et al.</i> , 2012
<i>Clonostachys Rosea</i>	(+) Plants					Li <i>et al.</i> , 2004
<i>Duddingtonia flagrans</i>	Sheep	None	+	None		Peña <i>et al.</i> , 2002
<i>Duddingtonia Flagrans</i>	Goats	None	+	+	None	Epe <i>et al.</i> , 2009
<i>Duddingtonia Flagrans</i>	Cattle	None	+	None	+	Sarkunas <i>et al.</i> , 2000
<i>Duddingtonia flagrans</i>	Horse	None	+		+	Fernández <i>et al.</i> , 1997
<i>Drechmeria coniospora</i>	<i>In vitro</i>	+				Santos and Charles, 1995
<i>Harposporium anguillulae</i>	Sheep	+				Charles <i>et al.</i> , 1996
<i>Bacillus thuringiensis</i>	Sheep	None	+	+		Baloyi, 2011
<i>Bacillus thuringiensis</i>	Cattle	+	+	+		Ciordia and Bizzell, 1996
<i>Bacillus thuringiensis</i>	<i>In vitro</i>	+	+			Kotze <i>et al.</i> , 2005

EPG= egg per gram of faeces; LPG= larvae per gram of faeces; WT= live weight; * = L3 from pasture; + = reduction in LPG; None= no effect

3.2. Medicinal Plants as Alternative to Chemotherapy

3.2.1. Use of plants as a source of phyto-medicines

Since the time immemorial, our traditional system of medicine and folklore claiming that medicinal plants as a whole or their parts are being used in all types of disease successfully including anthelmintics (Jitendra *et al.*, 2010). Plant-based drugs are believed to be less toxic to the host and end-users. They are easily available, biodegradable, cheaper and eco-friendly. Moreover, the people have used them for generations. Rural folk, tribes, ethnic groups and nomads have found several plants very effective for their day-to-day problems of health care. In livestock, medicinal plants are important in veterinary practice worldwide.

Therefore, Phytomedicines in veterinary practice have great potential as alternative medicine (Kumar *et al.*, 2008). Unlike synthetic anthelmintics, Herbal medicines with different mode of action could be of value in preventing the development of the resistance (Singh *et al.*, 2008)

Some devastating infectious diseases *such as* malaria, responsible for deaths of thousands of people can be overcome with traditional herbal anti-malarian drugs obtained from South America, Africa and Asia *ie.*, Cinchona (*Cinchona sp.*), Qing hao (*Artemisa annua*), Changshan (*Dichroa febrifuga*), Neem (*Azadirachta indica*), *Cryptolepis sanguinolenta* and other plants (Willcox *et al.*, 2005). Researchers around the world have scientifically explored the real effect of many

plants used as medicines whose uses are not validated by rigorous scientific experimentation. Many plants are being screened for anti-parasitic effects on animals; since animal behaviour reveals self medication when animals select and ingest some specific plants (Cousing and Huffman, 2002; Huffman, 2003). During the last decades the study of medical principles from plants has gained considerable interest and a number of natural bio-active compounds from plant extracts are currently commercially available to cure many diseases (Sumer and Plutkin, 2000). Sinha parol *et al.* (2012) reported that plants are one of the most important sources of medicines. The medicinal plants are rich in secondary metabolites which are potential sources of drugs and essential oils of therapeutic importance. The important advantages claimed for therapeutic uses of medicinal plants in various ailments are their safety besides being economical, effective and bioavailable.

3.2.2. Plant parts and methods of preparation of herbal medicine:

Methods of preparation of traditional medicines varies according to the active ingredient to be

extracted, the route of administration, and the medical intent For preparation of drugs, parts of the plants that are mostly utilized are roots, barks, wood, leaves, stems, flowers, fruits, juices, resins, latex, grains, buds, bulbs and seeds (Jabbar *et al.*, 2006a; Dilshad *et al.*, 2008).

Main methods used for processing the herbal remedies were; decoction, maceration, poultices and ointment. Decoction; this process was used when working with tough and more fibrous plants/ parts such as the trunk bark and root bark. The materials were boiled in water for long period of time to soften the materials and release the active chemical constituents. Maceration was preferably used for very tender/fresh plants, that were thought to lose their active compounds on heating. The mashed or ground plant materials were stirred in water to make a concoction. The poultices were prepared by mashing fresh plant materials. The mashed material would be applied directly on the affected part [Allan, 2011]. The processing of the herbal remedies is diagrammatically described below by Allan, 2011.

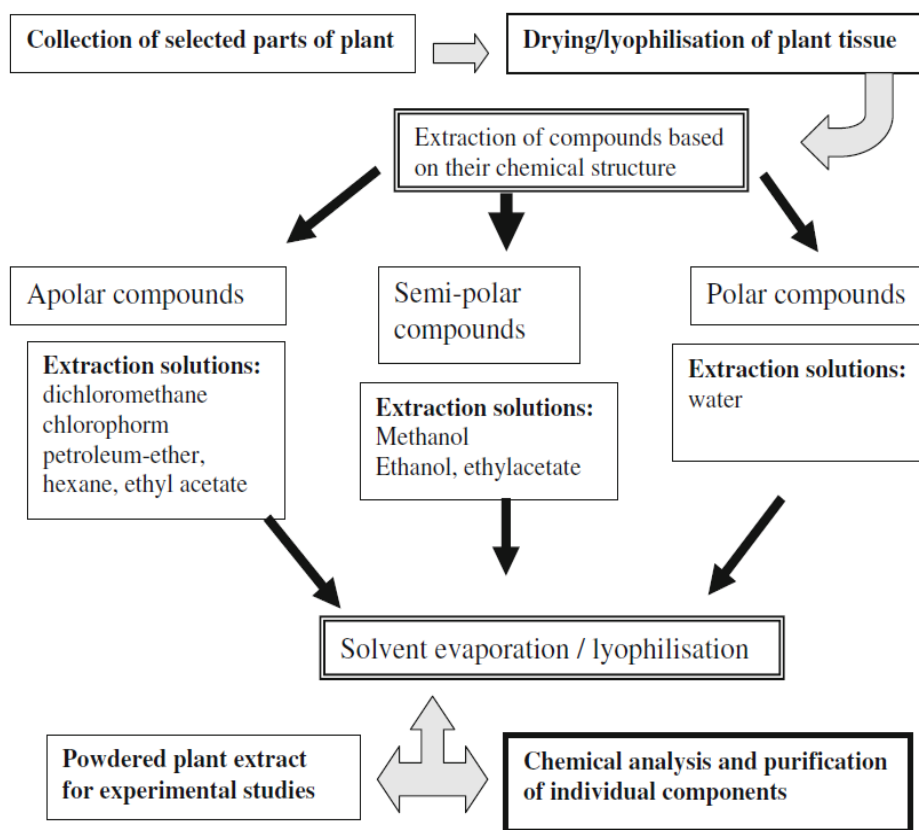


Figure2. Diagram showing the key steps of preparatory process for obtaining the single group of phytochemical /compound from the higher plants.

As there are many ways of plants preparation, dosage form, risk of side effects, scientific verifications, for therapeutic use different

authors has been described the preparation in various ways as indicated in table 4.

Table4. *Plants and plant preparations*

Botanical & Common Name	Preparation	Dosage	Risks, Side-effects & Effectiveness	Scientific Verification & Comment	Prime Source
Allium sativum Garlic	Crushed cloves	1 Tsp/ animal/day	No side-effects known, further investigation of effects on derogation of milk-flavour, Effective against GIN and lungworms	traditionally applied In vivo trial showed no effect of garlic administration contradicting statements of the effectiveness	Allen, 1998 Duval, 1994 Cabaret et al., 2002b Meat New Zealand, 1998 Perezgroves, no date University of Aberdeen, no date
	Dried powder	Mixed in with feed Dosage not specified			
	Juice	Oral drench Dosage not specified			
	Capsules	2-3 / animal/day			
Annonum senegalensis Custard Tree	Dried stem bark extract	Not specified for living animals	No toxicity noted	Traditionally used by Nigerian farmers In vitro test showed promising potential	Alawa et al., 2003
Artemisia abrotanum Southern	Powdered herbs	1 Tbs/ sheep/ twice daily for several days	No toxicity noted	Although traditionally used, activity	Hoffmann, 1995 in: Häublein, 2005

3.2.3. Exploring the anti-parasitic properties of plants

A wide range of plants and their products around the world are being explored to look for their possible anthelmintic effects on cestodes and trematodes (Abdel-Ghaffar et al., 2011), and against nematodes (Datsu Kalip et al., 2011). Due to the important economic impact of gastrointestinal parasitic nematodes in the livestock industry around the world, most of the research on plant extracts is being focused on searching bioactive compounds from plants against this important group of parasites.

Traditionally, some plants around the world are well known as anti-parasitic plants because they contain substances with anthelmintic effects against parasitic nematodes affecting agricultural crops (Krueger et al., 2009) or animal parasitic nematodes (De Jesús Gabino et al., 2010). Perhaps, the most known cases of plants with nematicidal properties around the world are garlic (*Allium sativum*) (Qadir et al., 2010) Marigold (*Tagetes erecta*) (Krueger et al., 2009).

Another example is the South African plant *Curtisia dentata* commonly used for ages by rural communities as a remedy to cure a number of diseases caused by bacteria and fungi in either human being or animals (Shai et al., 2008) and against animal parasitic nematodes (Shai et al., 2009). Nevertheless, every year, the

list of new plants with nematocidal *in vitro* and *in vivo* properties against animal parasites is growing as new natural alternatives for replacing (at least partially) the use of chemical drugs (Shai et al., 2009).

Some forage have been evaluated searching for potential bio-active compounds against sheep and goat parasitic nematodes with variable results. However studies must be intensified; since some individual limitations in application have been noticed; *ie.*, toxicity, metabolic disorders and inappropriate applications can cause severe damage and even the death of treated animals (Rahmann and Seip, 2008). Other plants are being investigated as bio-active forages in the control of *Haemonchus contortus* in lambs with good/moderate results. For instance Wormwood (*Artemisia absinthium*) which was offered to lambs for voluntary intake, parasitic burden was reduced almost in 50%. Additionally, faecal egg excretion expressed on a dry matter basis was also reduced by 73% in animals fed with the selected plant (Valderrábano et al., 2010).

Some plant extract have shown an extraordinary bio-activity against sheep parasitic nematodes; *ie.*, supplementing sheep with a *Fumaria parviflora* ethanol extract eliminated fecal eggs and caused 72 and 88% mortality of adult *Haemonchus contortus* and *Trichostrongylus colubriformis*, respectively (Hördegen et al.,

2003). These are only a few examples of candidate plant extracts to be used in the control of parasites in sheep and goat farming. Rochfort et al (2008) from Australia published a very complete and extraordinary review about bioactive plants and their impact on animal health and productivity. On the other hand, Diehl et al (2004) published the results of a very interesting research project evaluating eighty six plant extracts from Ivory Coast flora and finding that fifty percent of the evaluated plants had nematocidal activity against *Haemonchus contortus* larvae. Such results showed evidence about the important nematocidal activity of plants from Ivory Coast as potential ethnobotanical tools of control against ruminant parasitic nematodes (Diehl et al., 2004).

Some recent reports of nematocidal activity of plant extracts against ruminant parasites in different countries are described as follows: In Ethiopia, extracts from *C. macrostachyus* and *E. capensis* have shown promising *in vitro* anthelmintic activity against eggs and adult *H. contortus* which supports the traditional use of these plants as anthelmintic (Mihretabs et al., 2011). In Pakistan, *Adhatodavasic* both aqueous and ethanolic extracts exhibit an *in vitro* ovicidal and larvicidal activity ranging between 81-89% against diverse genera/specie of gastrointestinal parasitic nematodes of sheep (Al-Shaibani et al., 2008). In Burkina, Faso, two medicinal plants *Anogeissus leiocarpus* and *Daniellia oliveri* were analyzed to identify their anthelmintic effect against nematodes of sheep abomasum. *A. leiocarpus* and *D. oliveri* showed a maximum lethal activity, between 80 and 100%, respectively, against adult *Haemonchus contortus* (Aldama et al., 2009; Kaboure et al., 2009).

Many countries have developed important screening of plant extracts with anthelmintic properties from their native flora with an enormous potential for the control of animal parasitic nematodes with encouraging results. These countries *such as* Brazil, India, South Africa, China and others possesses an extraordinary richness in their medicinal flora and they have currently developed an important industry from plant extracts ably supported by science. Some researchers stand out for their important contributions in this regard: Githiori et al (2006) at the International Livestock Research Institute in Nairobi, Kenya; Iqbal et al (2001) and his group or researchers from the

Department of Veterinary Parasitology, University of Agriculture, Faisalabad, Pakistan have developed a solid package of information about a big list of native plants with encouraging results in the control of GI parasites (Bachaya et al., 2009).

3.2.4. Condensed tannin-rich plants

A number of research works have focused on the anthelmintic effect of tannin rich plants against GIN. This group of bio-active compounds present in selected plant material are being obtained from all over the world, from temperate areas well as from tropical tannin rich fodders (Alonso-Diaz et al., 2010).

Interdisciplinary groups of researchers (Hoste et al., 2006; Alonso Díaz et al., 2008; Calderón-Quintal et al., 2010; Martínez-Ortíz-de-Montellano et al., 2010) have developed important research studies on tannin-rich plants in the control of *H. contortus* and other important gastrointestinal nematodes. Most scientific works focused on identifying the bioactive compounds produced by nematocidal plants have reported the presence of different molecules including catechins, condensed tannins, flavonoids and steroids (Oliveira et al., 2009) and polyphenolics (Lorimer et al., 1996); as well as bio-active enzymes such as cystein protease and secondary metabolites such as alkaloids, glycosides and tannins (Athanasiadou and Kvriazakis, 2004). Further in-depth studies need to be undertaken since even though anti-parasitic properties are being demonstrated, negative effects such as reduction in food intake by animals have been identified and this should be considered before establishing their use as an alternative method of control (Githiori et al., 2006).

Up to date studies, researchers are reaching beyond the general knowledge about lethal *in vitro* activity of plants and bio-active compounds derived from selected plants against the most important nematode parasites of ruminants. New efforts are being carried out to find practical applications of plants or plant products in the control of ruminant parasitic nematodes; including ways and means of overcoming limitations in applications to animals (Rahmann and Seipa, 2008). Recently in Laos, reduction in appearance of nematode eggs on goat feces with the Cassava foliage

supplement has been demonstrated (Phengvichith and Preston, 2011). Some plant extracts used in vitro to control gastrointestinal

nematodes in animals around the world is discussed by different authors in the table below.

Table 5. Some plant extracts used in vitro to control gastrointestinal nematodes in animals around the world

Plant family	Plant scientific name	Country of Use	Method of Preparation	Claims	References
Asphodelaceae	<i>Aloe ferox</i>	South Africa	Leaf extract	Effective	Maphosa <i>et al.</i> , 2010
Liliaceae	<i>Allium sativum</i>	Pakistan	Water extract of the garlic bulb	Effective	Iqbal <i>et al.</i> , 2001
Moraceae	<i>Ficus spp.</i>	Not stated	Juice extract	Effective	Gillian <i>et al.</i> , 2004
Bromeliaceae	<i>Ananas comosus</i>	Pakistan Philippines	Raw powder	Ineffective	Hördegen <i>et al.</i> , 2003.
Zingiberaceae	<i>Zingiber officinale</i>	Pakistan	Ethanol extract of Rhizomes	Effective	Iqbal <i>et al.</i> , 2001
Leguminosae	<i>Tephrosia vogelli</i>	Ethiopia	Ethanol extract of leaves	Effective	Siamba <i>et al.</i> , 2007
Amaranthaceae	<i>Halothammus somaliensis</i>	Ethiopia	Crude preparation of roots powder	Effective	Dawo and Tibbo, 2005
Leguminosae	<i>Ornobrychis viciaefolia</i>	France	Aqueous acetone extract	Effective	Paolini <i>et al.</i> , 2003
Fabaceae	<i>Elephantorrhiza elephantina</i>	South Africa	Aqueous extract of leaves	Effective with high doses	Maphosa <i>et al.</i> , 2010
Mimosaceae	<i>Albizia anthelmintica</i>	East Africa, Kenya, Sweden, Ethiopia, Uganda	Heat treated or soaked in water	Ineffective	Longok, 2002

4. CONCLUSION AND RECOMMENDATIONS

Parasitic nematodes remain a major threat to the health and welfare of small ruminants all over the world and the demand for alternative control measures has constantly increased during the last years. Infestation with GIN parasites can have severe consequences for the animal as well as for the livestock farmers leading to economic loss and restricted productivity. The use of chemical anthelmintic drugs for controlling animal parasitic nematodes is rapidly losing popularity due to a number of disadvantages. Anthelmintic resistance in the parasites is spreading and the inefficacy of chemical anti-parasitic compounds is threatening animal health. New plants with medicinal properties against parasites of ruminants are being investigated around the world with promising results. When plant/plant extracts are being selected for use as anti-parasitic drugs in sheep a particular attention should be given to the fact that the bio-active compound could be found in stems, roots, leaves, flowers, fruits or even in the entire plant. This means that obtaining plant

extracts is a laborious and complex process. Also, the mode of extraction and the solvent used can determine the success in isolating the expected bioactive compounds; since a wide variety of compounds can be hidden into the structural parts of the plants and the only way they could be isolated is through exploring the use of a range of organic solvents. Therefore, in the near future natural products obtained from plants extracts seems that likely will become a viable alternative of control of parasitizes of veterinary importance. Although a lot of research has been done on biological control options the outcome of this area of investigation proved rather disillusioning.

Based on the aforementioned scientific information gathered, the following points could be recommended:

- ❖ Any approach related to the current parasite control options should be studied in detail taking into considerations of the global threats of drug resistance against many of the antihelmentiscs.

- ❖ Since promising results have already been documented on the use of biological control methods and medicinal plant products, further study must be intensified to produce, low cost but effective and user friendly control methods.

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