Alternative compounds to commercially available anthelmintics to be used in sheep and goats

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Introduction

Helminthosis (worm burdens) in small ruminants is a problem within itself in all agro-climatic zones of the world. In addition, anthelmintic resistance (AR) is a global problem that threatens the welfare of sheep and goats and represents a challenge in eroding the productivity of small ruminants, thus affecting the survival of the sheep/goat farms. Most economic losses are due to what is known as "sub-clinical nematodosis," which is not immediately observed and not even measured by sheep and goat ranchers. Jabbar et al., 2006 reviewed extensively the AR status in small ruminants. AR is identified when a previously used anthelmintic ceases to kill an exposed worm population at the therapeutically recommended dosage (Jabbar et al., 2006). In the United States, all the major groups of the commercially available anthelmintics have been reported to have developed variable degrees of resistance when used to protect small ruminants. One of the earlier reports on alternative use of plants with anthelmintic properties was presented by Kissam (1781) reporting that cow-itch (*Phaseolus zuratensis siliqua hirsuta)* could be used as a vermifuge to treat children with worms instead of preparations of mercury, aloes, rhubarb, jalap (a dried tuberous root from *Ipomoea purga* syn. *Exogonium purga,* a plant in the morning-glory family*)*, steel, tin, sulphur (sulfur)…"and others too tedious to mention". Kissam (1781) indicated that the hairy substance growing outside the pods was mixed with molasses or syrup and given to children and adults for 3 consecutive days at the rate of one teaspoon for children and double for adults. Efforts to reduce production losses caused by Gastrointestinal Nematode (GIN) parasitism in small ruminants (sheep and goats) have led to the investigation, development and implementation of a number of control methods to complement or replace commercially available anthelmintics. The need for alternative control measures stems from the development of anthelmintic-resistant GINs with reports of multi-class resistance to these drugs. The Anthelmintic Resistance (AR) has been very well documented all over the world. A number of these control methods such as predacious micro-fungi, protein supplementation, and plant parts or extracts in feed, additions to feed and vaccines have demonstrated potential to control infection but require development and examination under production conditions. In addition, demand for alternative dewormers originates from the organic small ruminant industry. Breeding for natural resistance to GIN infection has already shown success in controlling the infection under natural production conditions and that will be the topic for another occasion. In most cases researchers have used Packed Cell Volume (PCV) or hematocrit and Fecal Egg Count (FEC) as indicators of efficacy of the different tested compounds. This presentation will attempt to focus on *"alternative compounds"* to reduce GIN infection in sheep and goats. This effort started as a discussion on *"herbal anthelmintics",* however the body of documented instances of the use of such products is negligible; therefore it was expanded to the current concept.

Diatomaceous earth

Diatomaceous earth (DE) is a powdered, fossilized, geological siliceous deposit, rich in unicellular marine or fresh water diatoms, which damages the invertebrate cuticle (arthropods and nematodes), increasing permeability and causing death by dehydration (McLean et al., 2005). DE with less than 7% composition of crystalline silica is generally recognized as a safe feed additive in Canada and the USA (Bennett et al., 2011, Köster, H, 2013). DE is used to control many invertebrate pests, including grain storage invertebrate pests and as an alternative anthelmintic product fed to domestic animals (poultry, sheep and cattle) for gastro-intestinal parasite control, although the small number of efficacy studies show mixed results (Fernandez et al., 1998 and McLean et al., 2005, Bennett et al., 2011). When naturally infected goats (*Haemonchus contortus, Eimeria* and *Trichostrongylus spp.)* were fed DE at 50, 100 and 150 µg/kg body weight, Bernard (2009) reported that DE did not show an anthelmintic effect as expressed by eggs per gram of feces.

Condensed Tannins

Tannins are natural polyphenols. Biosynthetically the Condensed Tannins (CT) are formed by the successive condensation of the single building blocks, with a degree of polymerization between two and greater than fifty blocks being reached. The coupling pattern of the catechin units in condensed tannins can vary considerably (Khanbabaee and van Ree, 2001). In forages (mostly leguminous plants), tannins are considered secondary compounds and in general herbivores avoid plants with excess tannin content. However, it has been reported by many investigators that CTs have beneficial effects relative to parasitized sheep or goats eating plants with CTs because CTs aid in the management of GIN infestations (Min and Hart, 2003; Coffey, 2007; Lisonbee et al., 2009; Novobilský et al., 2001; Juhnke et al., 2012; . In the United States, several plants are of interest to sheep and goat producers: Sericea lespedeza (*Sericea cuneata*), birdsfoot trefoil (*Lotus corniculatus*), chicory (*Cichorium intybus*) and sainfoin (*Onobrychis viciifolia*). In other regions in the world plants of the genera *Acacia, Schinopsis, Leucaena, Salix* have shown to have anthelmintic activities (Minho et al., 2008; Beserra de Oliveira et al., 2011; Mupeyo et al., 2011). However, the effects of feeding high tannin containing feeds have not always reduced parasite burdens. For example, Whitley et al. (2009) reported that high tannin sorghum rations did not affect FEC or PCV of goats eating the high sorghum diets. Also, Max et al., (2007) reported a slight FEC reduction (only 19%) in sheep and goats fed up to 170 g/animal/day of acacia leaf meal (*Acacia polycantha*) compared to control groups. Use of CTs as alternative anthelmintic has multiple research trials backing up claims of efficacy and has encouraged producers to the use of lespedeza as a component of integrated parasite management plans.

Other "herbal dewormers" and anthelmintic compounds

At least two commercial herbal dewormers have been tested in research trials. Burke at al. (2009) did not find any indication, after a 112 day trial, that a commercially available herbal dewormer controlled GIN in goats. Yoder (2011) tested Plumbagin in sheep and reported that treated sheep and control sheep did not show any difference on parasite burden as expressed by PCV and FEC. Garlic, papaya seeds and pumpkin seeds have been used in trials with sheep and

goats and have not been found to enhance PCV or reduce FEC in the treated sheep and/or goats (Burke et al. 2009; Gooden 2012, Escobar et.al. unpublished data). However, Stickland et al. (2009) reported 64.4% reduction in FEC in sheep using garlic and 65.5% reduction in FEC when pumpkin seeds were fed. Diehl (2004) published an extensive report of 60 plants in the Ivory Coast that have shown larvicidal activity against *H. contortus*. Several parts of plants were extracted with 90% ethanol and 25.6% of the extracts showed a high activity. Oil and seed paste of *Chenopodium* spp. (epazote, wormseed, erva de Santa Maria) has been used to treat worm infections in animals and humans for centuries, however the margin of safety is very narrow and *Chenopodium* may cause adverse reaction and even death to the treated animals (Cornell University, 2013). Other relevant alternative plants are included in the enclosed table.

Discussion

The list of reports on the use of alternative anthelmintics for use in sheep and goats is overwhelming; however, the methods for analysis are ingenious but not standardized. It seems that the compounds tested may reduce larval activity in-vitro but when tested in-vivo the results from treated animals are not different than results from the control ones. One difficulty which is very common is the proper identification of the plants. The scientific name plus the variety should be included in reports. For example, pumpkin's scientific name is *Cucurbita pepo*; however there are at least 5 varieties commercially cultivated in the US. Another underlying situation exists when researchers need to decide between running an in-vitro trial or an in-vivo trial. Both complement each other providing information to better understand the results in the field and to make recommendations. Once more there is the need of collaborative studies and the contribution of chemists, botanists and animal scientists in order to identify alternative compounds to control worms in sheep and goats.

Table 1.- Reported relevant potential alternative natural anthelmintics used in small ruminants

Small Ruminant Species	Name of the Alternative Dewormer	Parasite species	Test Conducted	Results	Reference
Sheep	Jujube (Bark, crude methanolic extract) - *Ziziphus nummularia.*	*H. contortus*	In-vitro: • adult motility assay • egg hatch • larval development In-vivo	Effective 84.7 % FECR	Bachaya, et.al, 2009.
Sheep	*Acacia nilolitica*-pods with seeds - crude methanolic extract	*H. contortus*	In-vitro: • adult motility assay • egg hatch • larval development In-vivo	Effective 78.5 % FECR	Bachaya, et.al, 2009.
Sheep	*Chenopodium album*	*H. contortus*	In-vitro: • adult motility assay • egg hatch In-vivo, reduced FEC	Effective,LC_{50}=0.449 mg/mL 93.9% reduction	Jabbar et al., 2007
Sheep	*Caesalpinia crista*	*H. contortus*	In-vitro: • adult motility assay • egg hatch In-vivo, reduced FEC	Effective,LC_{50}=0.134 mg/mL 82.2% reduction	Jabbar et al., 2007
Sheep	Wormwood - *Artemisia absinthium*	*H. contortus*	In-vitro: • adult motility assay In-vivo, reduced FEC	Effective 80 to 83% reduction	Tariq et al., 2009
Sheep	Banana leaves	*H. contortus*	In-vitro: • adult motility assay In-vivo, reduced FEC	Reduced 97% larval development Reduced 58%	Oliveira et al. 2010

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