

# Anthelmintic activity of plants against gastrointestinal nematodes of goats: a review

Francianne Oliveira Santos<sup>1</sup>, Amanda Ponce Morais Cerqueira<sup>1</sup>,  
Alexsandro Branco<sup>2</sup>, Maria José Moreira Batatinha<sup>3</sup> and Mariana Borges Botura<sup>1</sup>

## Review

**Cite this article:** Oliveira Santos F, Ponce Morais Cerqueira A, Branco A, José Moreira Batatinha M, Borges Botura M (2019). Anthelmintic activity of plants against gastrointestinal nematodes of goats: a review. *Parasitology* **146**, 1233–1246. <https://doi.org/10.1017/S0031182019000672>

Received: 17 February 2019  
Revised: 26 April 2019  
Accepted: 29 April 2019  
First published online: 14 June 2019

### Key words:

Anthelmintic; gastrointestinal nematodes; goats; medicinal plants

### Author for correspondence:

Mariana Borges Botura,  
E-mail: [mbootura@uefs.br](mailto:mbootura@uefs.br)

<sup>1</sup>Laboratório de Toxicologia, Universidade Estadual de Feira de Santana, Av. Transnordestina s/n, CEP: 44036-900, Feira de Santana, BA, Brazil; <sup>2</sup>Laboratório de Fitoquímica, Universidade Estadual de Feira de Santana, Av. Transnordestina s/n, CEP: 44036-900, Feira de Santana, BA, Brazil and <sup>3</sup>Laboratório de Toxicologia, Hospital de Medicina Veterinária, Universidade Federal da Bahia, Av. Ademar de Barros, 500, Ondina, CEP: 40170-110, Salvador, BA, Brazil

## Abstract

The gastrointestinal nematodes (GIN) stand out as an important cause of disease in small ruminant, especially on goat farm. Widespread resistance to synthetic anthelmintics has stimulated the research for alternative strategies of parasite control, including the use of medicinal plants. The present work summarizes the *in vitro* and *in vivo* studies of plants with activity against GIN of goats, focusing on the description of chemical constituents related to this effect. This review retrieved 56 scientific articles from 2008 to 2018 describing more than 100 different plant species. The most frequently investigated family was Fabaceae (30.7%). Most *in vitro* studies on the activity of plant extracts and fractions were carried out with free-living stages nematodes. *In vivo* studies were conducted mainly with the use of plants in animal feed and generally showed lower effectiveness compared to *in vitro* assays. The main plant secondary metabolites associated with anthelmintic effect are condensed tannins, saponin and flavonoids. However, the studies with compounds isolated from plants and elucidation of their mechanisms of action are scarce. Herbal medicines are thought to be promising sources for the development of effective anthelmintic agents.

## Introduction

Gastrointestinal Nematodes (GIN) are an important cause of disease in small ruminant production worldwide, especially in tropical and subtropical countries. These parasites are responsible for substantial losses in productivity and can lead to mortalities and clinicopathological changes (Cantacessi *et al.*, 2012; Roeber *et al.*, 2013).

Goats and sheep are infected with the same GIN species, mainly *Haemonchus contortus*, *Trichostrongylus axei*, *Teladorsagia circumcincta* (abomasum), *T. colubriformis*, *Strongyloides papillosus*, *Nematodirus* spp. (small intestine), *Oesophagostomum columbianum* and *O. venulosum* (large intestine) (Hoste *et al.*, 2010; Bentounsi *et al.*, 2012; Moreno-Gonzalo *et al.*, 2013a). The nematode of major concern is *H. contortus*, a highly pathogenic parasite, because its blood-sucking feeding habits cause anemia, submandibular edema and lethargy. These infections promoted decrease in milk production, reduction of growth, weight loss, diarrhea, reproductive disorders and changes in carcass quality. In cases of massive infections, high mortality rates are observed (Molento *et al.*, 2011; Cantacessi *et al.*, 2012).

Goats are more susceptible to GIN probably due to a deficiency in the immune mechanism of parasite expulsion. Moreover, they metabolize anthelmintic drugs faster than do sheep, reducing the efficacy of anthelmintics when they are treated with the same dose recommended for sheep (Hoste *et al.*, 2010).

The most common method used to control GIN is the repeated use of synthetic anthelmintics. The main anthelmintic drugs used belong to the groups of benzimidazoles, imidazothiazoles, macrocyclic lactones (Hoste and Torres-Acosta, 2011), monepantel and derquantel (Kaminsky *et al.*, 2011). There are some disadvantages, such as the development of resistant populations, high cost, risk of environmental pollution and reduction of animal production due to low effectiveness (Adamu *et al.*, 2013). Drug inefficacy can be associated with many factors, such as incorrectly or badly managed/inadequately stored drug, dose level, inaccurately calculated weight and differences among animal species in pharmacokinetics (Torres-Acosta and Hoste, 2008).

Anthelmintic treatments are usually less effective in goats and could contribute to the nematode resistance. The goats are more susceptible than are sheep to gastrointestinal nematode infections with a higher production of worm eggs and elevated number of adult parasites in the gastrointestinal tract. These factors show that goats can be responsible for the dissemination of worm eggs from resistant nematodes in populations of small ruminants (Torina *et al.*, 2004).

In this context, the investigation of the antiparasitic activity of natural bioproducts can contribute to the development of alternative treatments and the reduction of the dependence on conventional chemotherapy (Santos *et al.*, 2017). The interest in their anti-parasitic properties

is increasing as illustrated by several reviews concerning ethnoveveterinary medicine in different continents (Hounzangbe-Adote *et al.*, 2005; De Medeiros *et al.*, 2018).

The scientific validation of plants with antiparasitic activity requires the conduction of *in vitro* and *in vivo* studies to determine its effectiveness. Several *in vitro* tests were used to screen plants with anthelmintic activity of plants at different stages of the parasite, such as egg hatch assay (EHA), larval development assay (LDA), larval feeding inhibition assay (LFIA), larval migration inhibition assay (LMIA), larval exsheathment inhibition assay (LEIA) and adult motility inhibition assay (AMIA). Some assays were developed for *in vitro* drug screening or drug resistance testing of parasitic stages (Borges and Borges, 2016).

The adult motility inhibition assay (AMIA) is the only *in vitro* test to evaluate the anthelmintic effects on the parasitic life stage of the nematode (adult worm), which is the target of synthetic anthelmintic drugs. However, this test presents some limitations as the need to euthanize an animal infected with GIN and the maintenance of nematodes in a CO<sub>2</sub> incubator (short time of parasite viability) (Hounzangbe-Adote *et al.*, 2005; Andre *et al.*, 2016).

The *in vitro* tests are characterized by low cost, rapid collection, good sensitivity, repeatability and their use of free-living stages (eggs, first- and third-stage larvae) and adult nematodes species. However, they are not able to evaluate host factors since the substances are applied directly on the parasite (O'Grady and Kotze, 2004; Borges and Borges, 2016).

The *in vivo* evaluation of anthelmintic efficacy is performed by the fecal egg count reduction test (FECRT) or controlled test. The FECRT provides an estimate of the reduction in the excretion of eggs after treatment, while in the controlled test the effectiveness is assessed by comparing the parasite burdens in the treated groups compared to the control group. The controlled test is the most reliable method, but also the most expensive analysis in terms of labor requirements and animal usage (Taylor *et al.*, 2002).

Most studies on the anthelmintic activity of plants in small ruminants were performed in sheep. However, the results obtained from studies with this species cannot be extrapolated to goats because of immunological, physiological and behavioral differences between sheep and goats (Torres-Acosta *et al.*, 2004). The aim of this study is to provide an overview of the anthelmintic properties of the plants against GIN of goats, as well as to identify bioactive constituents related to this effect.

## Methods

For the article collection, we used the databases PubMed (database of the National Library of Medicine of the United States of America) and Science Direct, the Elsevier scientific literature platform belonging to the RELX group. We considered all original articles published between 2008 and 2018 and that investigated the activity of plants and their derivatives in the treatment against GIN of goats. The search strategy was based on three descriptors: plants, gastrointestinal nematodes and goats.

The abstracts of the articles were analyzed and after the initial screening, all relevant studies were recovered in full-text and evaluated. Only studies investigating plant extracts, its fractions and isolated compounds against GIN of goats were considered for potential inclusion in the review. *In vitro* and *in vivo* studies were included. The methods of exclusion were based on the following criteria: studies in small ruminants without specifying the animal species, studies testing synthetic or commercial substances and studies that were not research articles (i.e. review articles, encyclopedia, correspondence and book chapters).

## Results

337 articles were recovered in the two databases. After screening, 56 studies that presented the research object were found, out of which 17 were referred on the PubMed platform, 26 on the Science Direct platform and 13 on both platforms. These duplicate studies were compared through authors, title, year and journal of publication. Figure 1 shows the Flowchart of the general characteristics in the selection process to recover these articles.

The years from 2012 and 2013 presented most scientific productions, with 8 publications each. As for the countries responsible for the publications, Brazil was the country with the largest number ( $n=14$ ), followed by the United States of America ( $n=10$ ) and Spain ( $n=6$ ).

Table 1 shows 28 *in vitro* studies on the effects of plants against the GIN of goats. 32 families and 78 plant species were evaluated in *in vitro* studies. While Table 2 shows 30 *in vivo* studies, we identified the citation of 41 plants belonging to 18 families. Only two papers presented *in vitro* and *in vivo* tests in the same study. Considering the number of articles analyzed, the most frequently investigated family was Fabaceae (46.42%), followed by Ericaceae (14.29%), Asteraceae (7.14%) and Rhamnaceae (5.35%). In this review, the *Lespedeza cuneata* (Fabaceae) and *Calluna vulgaris* (Ericaceae) were the most studied species (6 articles for each species).

The *in vitro* studies were carried out mainly with stages of free-living *Haemonchus contortus* (64.2%) and *Trichostrongylus* (35.7%) spp. Many plants exhibited *in vitro* anthelmintic activity at a lower concentration ( $EC_{50} < 1.0 \text{ mg mL}^{-1}$ ), such as *Calluna vulgaris*, *Erica cinerea*, *E. umbellata* (Ericaceae), *Acacia nilotica*, *A. raddiana* (Fabaceae), *Persea Americana* (Lauraceae) and *Digitaria insularis* (Poaceae). The ethyl acetate extracts of *C. vulgaris* and *E. cinerea* were active on different stages of GIN (egg, larvae L<sub>3</sub> and adult parasite) (Table 1).

The *in vivo* studies were characterized by the oral administration of the leaves (fresh, hay, meal), aqueous extract and oil of plants to goats infected naturally or experimentally with GIN. The duration of treatment ranged from 01 to 189 days. The efficacy parameter frequently evaluated was the reduction in EPG (90%), followed by recovery of adult parasites (16.7%).

The main plant secondary metabolites associated with anthelmintic effect are condensed tannins (68%), saponins (12.5%) and flavonoids (8.9%). This review showed that the evaluation of anthelmintic activity of isolated compounds on goat's parasites is scarce. Only two studies *in vitro* (7.4%) used commercial substances that are found in plants: the flavonoids (quercetin, rutin and epicatechin) and the saponins (escin and digitonin).

## Discussion

### *In vitro* studies of the anthelmintic activity of plants

Plants stand out as an important source of new candidates for anthelmintic drugs. Several *in vitro* tests, as egg hatch and larval migration, motility and exsheathment assays, have been used to identify plants with effect against the GIN of goats.

Studies show that many plants evaluated bear anthelmintic properties against different abomasal and small intestine nematodes. In this review, antiparasitic effects of plants vary depending on the plant species, stage, the nematode species and the parasitic stage. *Erica cinerea* was more active against eggs and L<sub>3</sub> of *T. columbriformis* than to inhibit the egg hatching and larvae exsheathment of abomasal parasites (*H. contortus* and *T. circumcincta*) (Moreno-Gonzalo *et al.*, 2013a, 2013b). The *Agave sisalana* and *Moringa oleifera* has greater ovicidal effect while *Acacia nilotica* and *A. raddiana* are more active against L<sub>3</sub> of GIN (Botura *et al.*, 2013; Zabr e *et al.*, 2017; De Medeiros *et al.*, 2018). These

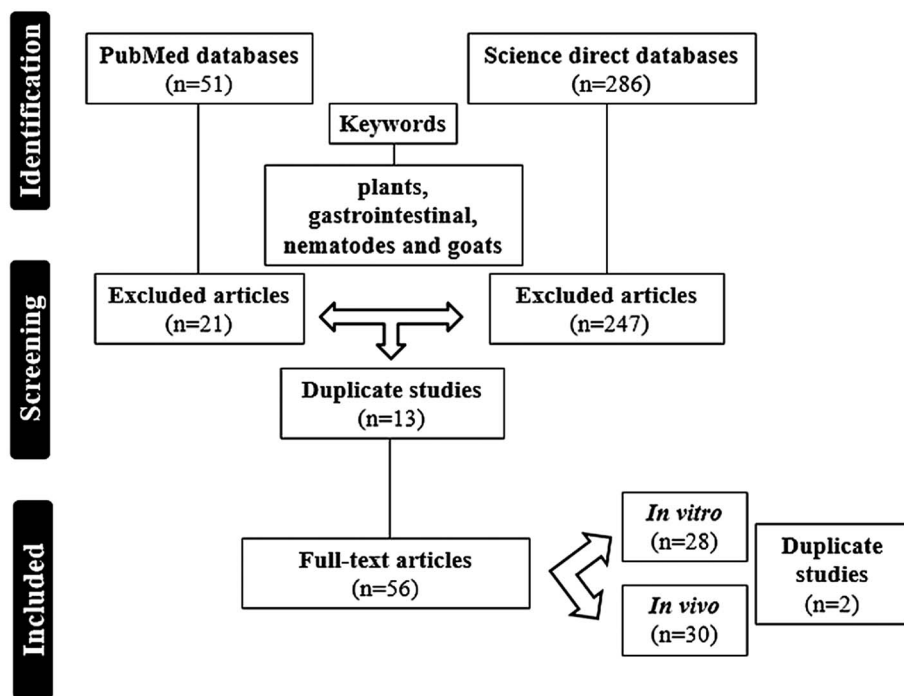


Fig. 1. Flowchart of the general characteristics for selection process of the articles.

variations can be related with differences in various enzymatic constituents and membrane structures of the species and nematodes' life stages. Plant secondary metabolites can act by means of different mechanisms such as: inhibition of egg hatching enzymes, competition with membrane receptors and binding to proteins in the membrane (Chan-Pérez *et al.*, 2016).

The use of standardized *in vitro* methods is essential for the assessment of the efficacy of plant products, particularly the determination of EC<sub>50</sub> and EC<sub>90</sub> (effective concentration 50% and 90%), which allows the comparison of activities of different plants (Borges and Borges, 2016). Adamu *et al.* (2013) established that a plant extract with EC<sub>50</sub> below 6 mg mL<sup>-1</sup> shows great anthelmintic potential. Considering this parameter, many plants recorded in this review have a promising antiparasitic effect. However, we found variations in the indices of efficacy for the same plant species, such as *Agave sisalana*, *Pistacia lentiscus*, *Calluna vulgaris* and *Erica umbellata*. This finding may be related to the type of preparation of the plant, stage and species of the parasite, contact and the time of exposure of the parasite to the vegetal product (Hernández-Villegas *et al.*, 2011). Some factors should be observed to avoid false positive or false negative results such as operator experience, choice of solvents, packaging and solubilization of plant products, quality of water and pH of the solutions used in the tests (Borges and Borges, 2016).

Variations in collection and preparation procedures of plant materials can interfere in the reproducibility of assays. Hence, chemical characterization of herbal products may be useful for the scientific validation of their antiparasitic activity. Phytochemical analyses using methods of mass spectrometry (liquid-chromatography mass spectrometry and gas-chromatography mass spectrometry) can aid in identifying the bioactive compounds found in plants (Hoste *et al.*, 2006).

In this review, it can be seen that anthelmintic activity of plants was evaluated mainly against stages of free-living nematodes (egg and larvae L<sub>3</sub>). Although the synthetic anthelmintic drugs act on the parasitic stages, the action on the stages of free-living nematodes can be useful for the control of helminths. Ovicidal action of plants can prevent parasitic development of the infective stage and reduce the pasture contamination (Silveira *et al.*, 2012). The evaluation of the activity of plant products against

different stages of parasites is necessary, since the action of phytochemicals can be different depending on the phases of the parasite's development (Borges and Borges, 2016).

The anthelmintic activity of medicinal plants has been related to secondary metabolites. The major classes of bioactive metabolites are flavonoids, alkaloids, coumarins, lignoids, triterpenes, saponins, polyphenols and tannins. The tannins are the most studied class of natural products for nematode control in small ruminants (Hoste and Torres-Acosta, 2011). The anthelmintic effect of tannins is attributed to its ability to bind to the proteins present in the cuticle, oral cavity, esophagus, cloaca and vulva of the nematodes, changing its physical and chemical properties. Another possibility is related to an indirect action of these compounds, which can enhance the host immune response due to its binding with proteins of the diet, protecting these substances from ruminal degradation and thereby increasing protein availability in the small intestine (Hoste *et al.*, 2006).

Several studies have showed the anthelmintic potential of the plants rich in condensed tannins. *In vitro* evaluations demonstrated effects of tanniferous plant extracts on the larval migration, larval artificial exsheathment, adult motility inhibition and egg hatching of *H. contortus* (Alonso-Díaz *et al.*, 2008; Moreno-Gonzalo *et al.*, 2013a; Naumann *et al.*, 2014). The use of polyvinylpyrrolidone (PVPP), an inhibitor of tannins, confirmed that this metabolite is responsible for the anthelmintic activity of the tanniferous plants (Alonso-Díaz *et al.*, 2008). The effect of larval exsheathment may be related to the presence of proline and hydroxiproline-rich proteins in the nematode larval sheath, cuticle and exsheathing fluid and these substances have high affinity for tannins. The exsheathment process is an important step, which is the transition from the free stage to the parasitic stage, allowing the larvae infection of the host (Alonso-Díaz *et al.*, 2011).

*In vitro* study with *Lysiloma latisiliquum* and *Onobrychis vicifolia*, rich in tannins, showed that the exposure of *H. contortus* (adult stage) to the extract acetone: water (70:30) of these plants led to changes in parasite structure: longitudinal and transversal folds and thicker cuticular ridges, aggregate material in the regions of the buccal capsule and anus or vulva. Alterations in cuticular structure can interfere with the movement of nematodes

Table 1. *In vitro* studies on the effects of plants against gastrointestinal nematodes

Family	Species	Part(s) used	Preparation	Parasite	Concentration (mg mL <sup>-1</sup> )	Active constituent	Results (EC <sub>50</sub> , IC <sub>50</sub> : mg mL <sup>-1</sup> )	Reference
Agavaceae	<i>Agave sisalana</i>	Waste	Juice	Gastrointestinal nematodes	39.3–146.3	Saponins	Reduction of larval counts (coproculture assay): >95%	Domingues et al. (2010)
	<i>Agave sisalana</i>	waste	A, EA, SF and FF	Gastrointestinal nematodes	0.02–10	Flavonoids and saponins	EHI: IC <sub>50</sub> : 4.7 (A), 0.1 (EA) and 0.05 (FF) LMI (%): 33.3 (A), 50.3 (EA) and 64 (SF)	Botura et al. (2013)
Anacardiaceae	<i>Pistacia lentiscus</i>	L	E (70%); E (100%); A (infusion)	<i>Teladorsagia circumcincta</i> , <i>Trichostrongylus colubriformis</i> and <i>Chabertia ovina</i>	0.0024–0.012	Phenolics (catechin, flavonolignosides, galloyl derivatives)	LEI: E (70%): 18.3–0.9 (semi log slope) E (100%) and A: Low larvicidal activity	Azaizeh et al. (2013)
				<i>T. circumcincta</i> and <i>T. colubriformis</i>	0.6–2.4	Phenolics (tannins, gallic acid)	LEI: 0–25%	Azaizeh et al. (2015)
Asteraceae	<i>Cichorium intybus</i> (two cultivars: Puna and Forage Feast)	L	ESL	<i>Haemonchus contortus</i>	1.67–10	Sesquiterpenes lactones (8-deoxylactucin)	EHI: EC <sub>50</sub> : 2.6 (Puna) and 6.4 (Forage Feast)	Foster et al. (2011)
	<i>Inula viscosa</i>	L	E (70%)	<i>T. circumcincta</i> and <i>T. colubriformis</i>	0.6–2.4	Phenolics (tannins, gallic acid)	LEI: 23–54%	Azaizeh et al. (2015)
Cupressaceae	<i>Juniperus pinchotii</i>	L	Rumen fluid with dried plant, fresh plant, oil	<i>H. contortus</i>	0.0001–0.006	Terpenoids and condensed tannins	LMI: Dried and Fresh Plant: 40–60% Oil: >60%	Armstrong et al. (2013)
Ericaceae	<i>Calluna vulgaris</i>	AP	Ac (70%)	<i>T. circumcincta</i> and <i>H. contortus</i>	0.075–1.2	Phenols (condensed tannins)	EHI: 20% ( <i>T. circumcincta</i> and <i>H. contortus</i> ). LEI: EC <sub>50</sub> = 0.61 ( <i>T. circumcincta</i> ) and 0.19 ( <i>H. contortus</i> ). AMI ( <i>T. circumcincta</i> ): 90% (+40 h exposure)	Moreno-Gonzalo et al. (2013a)
				<i>T. colubriformis</i>	0.075–1.2	Phenols (condensed tannins)	EHI: EC <sub>50</sub> = 0.52 (Ac 70%) LEI: EC <sub>50</sub> = 0.57 (Ac 70%), 0.07 (CTF) AMI ( <i>T. colubriformis</i> ): 90% (+90 h exposure) (Ac 70%)	Moreno-Gonzalo et al. (2013b)
				<i>T. circumcincta</i> and <i>H. contortus</i>	0.075–1.2	Phenols (condensed tannins)	EHI (%): 45 ( <i>T. circumcincta</i> ) and 30 ( <i>H. contortus</i> ) LEI: EC <sub>50</sub> = 0.21 ( <i>T. circumcincta</i> ) and 0.22 ( <i>H. contortus</i> ) AMI ( <i>T. circumcincta</i> ): 75% (+40 h exposure)	Moreno-Gonzalo et al. (2013a)
	<i>Erica cinerea</i>	AP	Ac (70%), CTF	<i>T. colubriformis</i>	0.075–1.2	Phenols (condensed tannins)	EHI: EC <sub>50</sub> = 0.34 (Ac 70%) LEI: EC <sub>50</sub> < 0.15 (Ac 70%), 0.108 (CTF) AMI ( <i>T. colubriformis</i> ): 70% (+90 h exposure) (Ac 70%)	Moreno-Gonzalo et al. (2013b)
	<i>Erica umbellata</i>	AP	Ac (70%)	<i>T. circumcincta</i> and <i>H. contortus</i>	0.075–1.2	Phenols (condensed tannins)	EHI: 10–20% ( <i>T. circumcincta</i> ) and 10–30% ( <i>H. contortus</i> ). LEI: EC <sub>50</sub> = 0.77 ( <i>T. circumcincta</i> ) and 0.179 ( <i>H. contortus</i> ). AMI ( <i>T. circumcincta</i> ): >90% (+40 h exposure)	Moreno-Gonzalo et al. (2013a)

<i>Erica umbellata</i>	AP	Ac (70%), CTF	<i>T. colubriformis</i>	0.075–1.2	Phenols (condensed tannins)	EHI: EC <sub>50</sub> = 0.121 (Ac 70%) LEI: EC <sub>50</sub> < 150 (Ac 70%) AMI ( <i>T. colubriformis</i> ): 70% (+ 70 h exposure) (Ac 70%)	Moreno-Gonzalo et al. (2013b)
Association of <i>C. vulgaris</i> , <i>E. cinerea</i> , <i>E. umbellata</i>	AP	Ac (70%)	<i>T. circumcincta</i> and <i>H. contortus</i>	0.075–1.2	Phenols (condensed tannins)	EHI: 80% ( <i>T. circumcincta</i> ) and 10–15% ( <i>H. contortus</i> ) LEI: EC <sub>50</sub> = 0.696 ( <i>T. circumcincta</i> ) and 0.253 ( <i>H. contortus</i> ) AMI ( <i>T. circumcincta</i> ): 100% (+ 20 h exposure)	Moreno-Gonzalo et al. (2013a)
Association of <i>C. vulgaris</i> , <i>E. cinerea</i> , <i>E. umbellata</i>	AP	Ac (70%), CTF	<i>T. colubriformis</i>	0.075–1.2	Phenols (condensed tannins)	EHI: EC <sub>50</sub> = 0.791 (Ac 70%) LEI: EC <sub>50</sub> < 150 (Ac 70%), 0.39 (CTF) AMI ( <i>T. colubriformis</i> ): 100% (+ 70 h exposure) (Ac 70%)	Moreno-Gonzalo et al. (2013b)
<i>Manihot esculenta</i>	L	M (80%)	<i>T. circumcincta</i>	3.1–50	–	M (50 mg mL <sup>-1</sup> ): EHI: 43.97–45.67% LDI: 97.11–98.96% LMI: 39.44–44.31%	Al-Rofaai et al. (2012a)
<i>Manihot esculenta</i>	L	M (80%)	<i>T. colubriformis</i>	3.1–50	Tannin condensed	EHI: LC <sub>50</sub> = 50.08–55.67 Larvicidal activity: LC <sub>50</sub> : L <sub>1</sub> : 16.07–16.89 L <sub>3</sub> : 81.40 (susceptible) and 101.80 (resistant)	Al-Rofaai et al. (2012b)
<i>Acacia angustissima</i> var <i>hirta</i> (STX)	L	Rumen fluid	<i>H. contortus</i>	–	Condensed tannins	LMI < 45%	Naumann et al. (2014)
<i>Acacia angustissima</i> var <i>hirta</i> (STP5)	L	Rumen fluid	<i>H. contortus</i>	–	Condensed tannins	LMI < 45%	Naumann et al. (2014)
<i>Acacia nilotica</i>	L	A and Ac	<i>H. contortus</i>	0.15–5.0	Phenolics (condensed tannins)	EHI: IC <sub>50</sub> > 5 (A and Ac) LEI: IC <sub>50</sub> = 0.195 (A) and 0.224 (Ac)	Zabré et al. (2017)
<i>Acacia pennatula</i>	L	Ac:A	<i>H. contortus</i>	1.2	Tannins	LMI: 43% LEI: 97%	Alonso-Diaz et al. (2008)
<i>Acacia raddiana</i>	L	A and Ac	<i>H. contortus</i>	0.15–5.0	Phenolics (condensed tannins)	EHI: IC <sub>50</sub> : 1.36 (A) and 0.68 (Ac) LEI: IC <sub>50</sub> : 0.331 (A) and 0.207 (Ac)	Zabré et al. (2017)
<i>Arachis glabrata</i>	L	Rumen fluid	<i>H. contortus</i>	–	Condensed tannins	LMI < 45%	Naumann et al. (2014)
<i>Desmanthus illinoensis</i>	L	Rumen fluid	<i>H. contortus</i>	–	Condensed tannins	LMI < 45%	Naumann et al. (2014)
<i>Hedysarum carnosum</i>	WP	Ac (70%)	<i>H. contortus</i>	0.15–1.2	Phenols (condensed tannins)	LEI: 25.67–98.44%	Aissa et al. (2016)
<i>Lespedeza cuneata</i>	L	Rumen fluid	<i>H. contortus</i>	–	Condensed tannins	LMI < 45%	Naumann et al. (2014)
<i>Lespedeza stuevei</i>	L	Rumen fluid	<i>H. contortus</i>	–	Condensed tannins	LMI: 60–65%	Naumann et al. (2014)
<i>Leucaena leucocephala</i>	L	Ac:A	<i>H. contortus</i>	1.2	Tannins	LMI: 44% LEI: 89%	Alonso-Diaz et al. (2008)

(Continued)

Table 1. (Continued.)

Family	Species	Part(s) used	Preparation	Parasite	Concentration (mg mL <sup>-1</sup> )	Active constituent	Results (EC <sub>50</sub> , IC <sub>50</sub> : mg mL <sup>-1</sup> )	Reference
	<i>Leucaena retusa</i> Benth.	L	Rumen fluid	<i>H. contortus</i>	-	Condensed tannins	LMI: 65.4%	Naumann <i>et al.</i> (2014)
	<i>Lysiloma latisiliquum</i>	L	Ac:A	<i>H. contortus</i>	1.2	Tannins	LMI: 33% LEI: 95%	Alonso-Diaz <i>et al.</i> (2008)
	<i>L. latisiliquum</i> <i>Onobrychis vicifolia</i>	L	Ac:A (70:30)	<i>H. contortus</i>	1.2	Condensed tannins	Structural changes in adult parasite: longitudinal and transversal folds; thicker cuticular ridges, material aggregates (buccal capsule and/or vulva or anus)	Martinez-Ortiz-de-Montellano <i>et al.</i> (2013)
	<i>O. vicifolia</i>	Hay	Ac (70%)	<i>T. circumcincta</i> <i>H. contortus</i>	0.3-1.2	Condensed tannins	LEI (%): 47.9 ( <i>T. circumcincta</i> ) 87.17 ( <i>H. contortus</i> )	Brunet <i>et al.</i> (2008a)
	<i>O. vicifolia</i>	Hay	A	<i>H. contortus</i> and <i>T. colubriformis</i> ,	1.2	Condensed tannins	No significant structural changes were detected.	Brunet <i>et al.</i> (2011)
	<i>Piscidia piscipula</i>	L	Ac:A	<i>H. contortus</i>	1.2	Tannins	LEI: 95%	Alonso-Diaz <i>et al.</i> (2008)
	<i>Prosopis juliflora</i>	Pods	EA and AF	<i>Haemonchus</i> spp. <i>Trichostrongylus</i> spp. and <i>Oesophagostomum</i> spp.	0.79-4.0	Alkaloids	EHI: IC <sub>50</sub> = 1.9; IC <sub>90</sub> : 2.9 (EA) IC <sub>50</sub> = 1.1; IC <sub>90</sub> : 1.43 (AF) No activity on larval migration and motility	Lima <i>et al.</i> (2017)
	<i>Bowditchia virgilioides</i>	R	Flavonoids isolated	<i>Haemonchus</i> spp. <i>Oesophagostomum</i> spp. and <i>Trichostrongylus</i> spp.	1	Isocordoin and cordoin + isocordoin	Low ovicidal and larvicidal activity	Santos <i>et al.</i> (2018)
Grossulariaceae	<i>Ribes nigrum</i>	L		<i>H. contortus</i>	Fr: 0.0375-0.6 quercetin and luteolin: 30 and 60 µM	Condensed Tannins	LEI: EC <sub>50</sub> Fr: 0.277 Fr + Quercetin: 0.137 (60 µM), 0.164 (30 µM) Fr + luteolin: 0.0312 (60 µM), 0.170 (30 µM)	Klongsirwet <i>et al.</i> (2015)
	<i>Ribes rubrum</i>	L		<i>H. contortus</i>	Fr: 0.0375-0.6 quercetin and luteolin: 30 and 60 µM	Condensed Tannins	LEI: EC <sub>50</sub> Fr: 0.126 Fr + Quercetin: 0.0788 (60 µM)	Klongsirwet <i>et al.</i> (2015)
Lauraceae	<i>Persea americana</i>	S	E and H	<i>H. contortus</i>	1	condensed tannins, flavonoids	LMI: E: EC <sub>50</sub> = 0.036 (Dried) and 0.147 (Fresh) H: EC <sub>50</sub> = 0.077 (Dried) and 0.801 (Fresh)	Soldera-Silva <i>et al.</i> (2018)
Malvaceae	<i>Tilia</i> spp.	Fl	CTF	<i>H. contortus</i>	Fr: 0.0375-0.6 quercetin and luteolin: 30 and 60 µM	Condensed Tannins	LEI: EC <sub>50</sub> Fr: 0.356 Fr + Quercetin: 0.0624 (60 µM), 0.156 (30 µM) Fr + luteolin: <0.0375 (60 µM), 0.0759 (30 µM)	Klongsirwet <i>et al.</i> (2015)

Meliaceae	<i>Azadirachta indica</i>	L	H, C, EA and M (80%)	<i>T. circumcincta</i>	3.1 to 50	Tannin	M (80%): -EHI: IC <sub>50</sub> = 44.2 (susceptible strain) IC <sub>50</sub> = 47.7 (resistant strain) -LDI: IC <sub>50</sub> = 7.15 (susceptible strain) IC <sub>50</sub> = 7.32 (resistant strain) -LMI: IC <sub>50</sub> = 24.91 (susceptible strain) IC <sub>50</sub> = 35.03 (resistant strain) H,C and EA: Low ovicidal and larvicidal activity	Al-Rofaai et al. (2012b)
Moringaceae	<i>Moringa oleifera</i>	S	A	<i>Strongyloides genera, Oesophagostomum spp., Haemonchus spp. and Trichostrongylus spp.</i>	1.95–250	Lectin	EHI: 40.4% LEI (L <sub>1</sub> and L <sub>3</sub> ): EC <sub>50</sub> = 0.078	De Medeiros et al. (2018)
	<i>Moringa oleifera</i>	S	A and E	<i>H. contortus</i>	0.95–15.6	Tannins, saponins, Alkaloids, flavonoids and terpenoids	EHI: IC <sub>50</sub> = 2.91 (E); 3.83 (A) LEI: IC <sub>50</sub> = 6.96 (E); 4.12 (A)	Cabardo and Portugalza (2017)
Myrtaceae	<i>Eucalyptus staigeriana</i>	L	EO	<i>H. contortus</i>	0.08–5.4	Limonene and citral	EHI: IC <sub>50</sub> = 0.324 LDI: IC <sub>50</sub> = 1.7	Macedo et al. (2010)
Oleaceae	<i>Phillyrea latifolia</i>	L	E (70%); E (100%); A (infusion)	<i>T. circumcincta, T. colubriformis and Chabertia ovina</i>	0.012–0.12	Phenolics (catechin, flavonoglucosides, galloyl derivatives)	LEI: E (70%): 21.1–1.4 (semi log slope) E (100%) and A: Low larvicidal activity	Azaizeh et al. (2013)
	<i>Phillyrea latifolia</i>	L	E (70%)	<i>T. circumcincta and T. colubriformis</i>	0.6–2.4	Phenolics (tannins, gallic acid)	LEI: 47–57%	Azaizeh et al. (2015)
Poaceae	<i>Digitaria insularis</i>	L	Extracts (HE, EA, B and RH) Fractions of EA (FR1 to FR6)	<i>H. contortus, Oesophagostomum spp. Trichostrongylus spp.</i>	0.08–2.5	Flavones (tricin and diosmetin)	EHI: all extracts and FR2 and FR3 (>90%). EC <sub>50</sub> = 0.7 (EA) EC <sub>50</sub> = 0.27 (FR2) No activity on larval motility	Santos et al. (2017)
Rhamnaceae	<i>Zizyphus joazeiro</i>	B	H, EA, SF and BA	<i>H. contortus, Oesophagostomum spp. and Trichostrongylus spp.</i>	0.5–4.0	Saponins	EHI: H: 48%, BA: 17%; EC <sub>50</sub> = 1.9 (EA) and 1.3 (SF) No activity on larval migration and motility	Gomes et al. (2016)
	<i>Zizyphus jujuba</i>	L	A	<i>H. contortus</i>	0.1–1.75	–	EHI: IC <sub>50</sub> = 0.302, IC <sub>90</sub> = 0.849 Adult assay: IC <sub>50</sub> = 0.943, IC <sub>90</sub> = 2.05	Preet and Tomar (2017)
Saltaceae	<i>Salix caprea</i>	L		<i>H. contortus</i>	Fr: 0.0375–0.6 quercetin and luteolin: 30 and 60 µM	Condensed Tannins	LEI: EC <sub>50</sub> Fr: 0.394 Fr+ Quercetin: 0.103 (60 µM)	Klongsriwet et al. (2015)
Various families	Various species	L and P	E (70%)	<i>T. circumcincta and T. colubriformis</i>	0.125 to 1.0 mg mL <sup>-1</sup>	Phenolics and tannins	LEI: 7–94%	Jamous et al. (2017)

Parts used: AP, Aerial Part; B, bark; L, leaf; Fl, Flower; Fr, Fruit; R, Root; S, Seed; ST, Stem; WP, Whole Plant.  
 Extracts: A, Aqueous; Ac, Acetone; EA, Ethyl Acetate; B, Butanol; C, Chloroform; D, Dichloromethane; E, Ethanol; HE, Hydroethanol; RH, Residual Hydroethanol; M, Methanol; H, hexane; EO, Essential Oil; ESL, Extract Rich in Sesquiterpene Lactones; CTF, Condensed Tannins Fraction; FGF, Flavonol Glycosides Fraction; SF, saponins fraction; FF, flavonoids fraction; AF, alkaloid-rich fraction; BA, betulinic acid; SA, Succinic acid.  
 Egg hatch inhibition (EHI), Larval development inhibition (LDI), Larval migration/motility inhibition (LMI), Larval exsheathment inhibition (LEI), Adult motility inhibition (AMI)

**Table 2.** *In vivo* studies on anthelmintic activity of plants in goats infected with gastrointestinal nematodes

Family	Species	Part used	Preparation	Treatment	Active constituent	Results	Reference
Agavaceae	<i>Agave sisalana</i>	Waste	Juice	0.92 g kg <sup>-1</sup> during 4–8 days	Saponins	No effect in EPG and worm burn Reduction in FLC: 95%	Domingues <i>et al.</i> (2010)
	<i>Agave sisalana</i>	Waste	Aqueous extract	1.7 g kg <sup>-1</sup> per 8 days	Saponins	Reduction of EPG (50.3%) No effect in worm burden	Botura <i>et al.</i> (2011)
Alliaceae	<i>Allium sativum</i>	Bu	Juice	40 mL or 3 bulbs animal <sup>-1</sup> per 7 days	–	No effect (EPG)	Burke <i>et al.</i> (2009a)
Anacardiaceae	<i>Pistacia lentiscus</i>	L	Fresh leaves	<i>Ad libitum</i> per 24 days	Condensed tannins	Reduction of EPG (low value)	Landau <i>et al.</i> (2010)
Asphodelaceae	<i>Aloe ferox</i> (Mill).	L	Extract powder	250 and 500 mg kg <sup>-1</sup> (9 days)	Amino acids and saponins	Reduction of EPG (38.75–48.79%)	Maphosa and Masika (2012a)
Asteraceae	<i>Viguiera dentata</i>	L	Fresh Leaves	<i>Ad libitum</i> for 1 h daily/10 days	Condensed Tannins	Reduction of EPG (91.17%)	Ventura-Cordero <i>et al.</i> (2017)
Casuarinaceae	<i>Casuarina cunninghamiana</i>	L	Fresh	<i>Ad libitum</i> per 8 days	Polyphenols Tannins	Lower reduction of egg output and larvae recovered from faecal cultures No effect in worm burden	Moreno <i>et al.</i> (2012)
Ericaceae	<i>Calluna vulgaris</i>	L	Hay	30–40 g DM kg BW <sup>-0.75</sup> per day for 11 weeks	Condensed tannins	Preventive: Reduction of EPG (14%) Curative: Reduction of EPG (47–66%)	Moreno-Gonzalo <i>et al.</i> (2014)
	<i>Erica spp. or Calluna vulgaris</i> (heather)	L	Fresh Leaves	Twice per week ( <i>ad libitum</i> )	Condensed tannins	No effect (EPG)	Osoro <i>et al.</i> (2009)
Ericaceae	<i>Erica spp. or Calluna vulgaris</i> (heather)	L	Fresh Leaves	0.5 kg head <sup>-1</sup> day <sup>-1</sup>	Condensed tannins	Reduction of EPG (50.64%)	Celaya <i>et al.</i> (2010)
	<i>Erica spp. or Calluna vulgaris</i> (heather)	L	Hay	30 g DM kg BW <sup>-0.75</sup> per day for 3 weeks	Condensed tannins	Reduction of EPG (40–50%)	Moreno-Gonzalo <i>et al.</i> (2013c)
Euphorbiaceae	<i>Manihot esculenta</i>	L	Fresh and silage	<i>Ad libitum</i> (21 days)	–	Reduction of EPG: ~42.13% (fresh) and ~10.11 (silage)	Sokerya <i>et al.</i> (2009)
Fabaceae	<i>Acacia karroo</i>	L	Fresh leaves	200 g head <sup>-1</sup> day <sup>-1</sup>	Polyphenols (condensed tannins)	Reduction of FLC (±80%) RAW: 90%.	Marume <i>et al.</i> (2012)
	<i>Acacia mearnsii</i>	B	Commercial extract	24 g animal <sup>-1</sup> per 27 weeks	Condensed tannins	Reduction of EPG (first half of the treatment) Worm burden: no change	Costa-Junior <i>et al.</i> (2014)
Fabaceae	<i>Acacia nilotica</i>	L	Fresh	<i>Ad libitum</i> per 8 days	Polyphenols	Lower reduction of egg output and larvae recovered from faecal cultures No effect in worm burden	Moreno <i>et al.</i> (2012)
	<i>Bauhinia pulchella</i>	L	Concentrate	180 mg kg <sup>-1</sup> per 63 days	Condensed tannins	No significant reduction in EPG Reduction on worm egg hatchability	Lopes <i>et al.</i> (2016)
Fabaceae	<i>Desmodium intortum</i>	L	Chopped	350 g day <sup>-1</sup> (98 days) 10 g PEG 6,000	Condensed tannins	Reduction of EPG (91.3%) compared to the group receiving PEG	Debela <i>et al.</i> (2012)
	<i>Elephantorrhiza elephantina</i>	R	Extract powder	250 mg kg <sup>-1</sup> and 500 mg kg <sup>-1</sup> (9 days)	Tannins	Reduction of EPG (22.22–64.19%)	Maphosa and Masika (2012a)



<i>Elephantorrhiza elephantina</i>	R	Aqueous fractions	12.5 to 75 mg mL <sup>-1</sup> dosed at 2 mL per 10 kg for 2 months	Condensed tannins	Reduction of EPG: 81.7 to 98.6%	Maphosa and Masika (2012b)
<i>Lespedeza cuneata</i>	L	Leaf meal	75 and 95% SL leaf meal pellets and a commercial pellet, all fed at 0.91 kg head <sup>-1</sup> day <sup>-1</sup> per 3 months	Condensed tannins	Reduction of EPG: 75–95%. RAW: 31–93.5% ( <i>H. contortus</i> ), 47% (at 95%SL) ( <i>T. circumcincta</i> ) (at 95%SL) 32.3% ( <i>T. colubriformis</i> )	Gujja et al. (2013)
<i>Lespedeza cuneata</i>	L	Hay	75% diet per 6 weeks	Condensed tannins	Reduction of EPG (91.9%) and the number of abomasal nematodes (74%)	Terrill et al. (2009)
<i>Lespedeza cuneata</i>	L	Fresh Leaves	0.45 kg head <sup>-1</sup> d <sup>-1</sup> (first 4 weeks), and 0.27 kg head <sup>-1</sup> d <sup>-1</sup> (final 4 weeks)	Condensed tannin	Reduction of EPG (82.4%) RAW: 52%	Mechineni et al. (2014)
<i>Lespedeza cuneata</i>	L	Leaf meal	Feeding: 90% leaf meal pellets (stored less than 6 months and 3 years)/28 days	Condensed tannins;	Reduction of EPG (66.2–79.2%)	Komimuru et al. (2014)
<i>Lespedeza cuneata</i>	L	Pellets (75% <i>S. lespedeza</i> )	<i>Ad libitum</i> per 28 days	Condensed tannins	Reduction of EPG (58%) No effect in worm burden (abomasal) Cuticular surface damage in adult <i>H. contortus</i>	Komimuru et al. (2015)
<i>Leucaena leucocephala</i> <i>Mimosa bahamensis</i>	L	Fresh Leaves	<i>Ad libitum</i> for 1 h daily per 10 days	Condensed tannins	Reduction of EPG (91.17%)	Ventura-Cordero et al. (2017)
<i>Lysiloma latisiliquum</i>	L	Fresh leaves	28 days post infection: 800 g per 7 days	Tannin	Structural differences on the cuticle and a lesser extent the buccal capsule.	Martinez-Ortiz-de-Montellano et al. (2013)
<i>Lysiloma latisiliquum</i>	L	Fresh leaves	10 g kg <sup>-1</sup> for 6 days	Condensed tannins	RAW: <i>H. contortus</i> (57%), <i>T. colubriformis</i> (64.3%)	Brunet et al. (2008b)
<i>Mimosa caesalpinhiifolia</i>	L	leaf powder	64.3–128.7 mg of CT per kg BW per day (21 days)	Condensed Tannins	Reduction of EPG: 28.9 to 51.6% to 28.9% RAW: 57.7%	Brito et al. (2018)
<i>Onobrychis vicifolia</i>	L	Hay	28 days post infection: <i>Ad libitum</i> per 7 days	Tannin	No significant structural changes were detected.	Martinez-Ortiz-de-Montellano et al. (2013)
<i>Quercus leucotricophora</i>	L	Roughage	Feeding: 70% per 120 days	Condensed tannins	Reduction of EPG (± 80%)	Raju et al. (2015)
<i>Quercus semecarpifolia</i>	L	Roughage	Feeding: 70% per 120 days	Condensed tannins	Reduction of EPG (± 80%)	Raju et al. (2015)
<i>Sesbania sesban</i>	L	Hay	220 g day <sup>-1</sup> (98 days)	Condensed tannins	Reduction of EPG (52.6%)	Debela et al. (2012)
<i>Leonotis leonurus</i>	L	Extract powder	250 mg kg <sup>-1</sup> and 500 mg kg <sup>-1</sup> (9 days)	Alkaloids, saponins and tannins	Reduction of EPG (47.26–80.62%)	Maphosa and Masika (2012a)
<i>Eucalyptus staigeriana</i>	L	Essential oil	500 mg kg <sup>-1</sup> (single dose)	Limonene and citral	Reduction of EPG (76.6%)	Macedo et al. (2010)
<i>Eucalyptus corymbia</i> , <i>Eucalyptus drepanophylla</i>	L	Fresh	<i>Ad libitum</i> per 8 days	Polyphenols	Lower reduction of egg output and larvae recovered from faecal cultures No effect in worm burden	Moreno et al. (2012)
Phytolaccaceae	L	Ethanol extract	250 mg kg <sup>-1</sup> per 2 days	Saponins, coumarins, flavonoids, steroids, terpenoids	Reduction of EPG (72%)	Hernández-Villegas et al. (2012)

(Continued)

Table 2. (Continued.)

Family	Species	Part used	Preparation	Treatment	Active constituent	Results	Reference
Poaceae	<i>Sorghum bicolor</i>	G	Grain	<i>Ad libitum</i> 14 × 10 <sup>3</sup> days	Condensed tannins	No effect in EPG	Whitley <i>et al.</i> (2009)
	<i>Zea mays</i>	G	Grain	Supplement 108: 108 g d <sup>-1</sup> Supplement 1%: 1% BW Supplement 1.5%: 1.5% BW	-	Supplement 1.5%: reduction of EPG (55.57%) Supplement 108 and 1%: no effect in EPG	Gárate-Gallardo <i>et al.</i> (2015)
Polygonaceae	<i>Gymnopodium floribundum</i>	L	Fresh Leaves	<i>Ad libitum</i> for 1 h daily per 10 days	Condensed Tannin	Reduction of EPG (91.17%)	Ventura-Cordero <i>et al.</i> (2017)
Asteraceae, Alliaceae, Apiaceae, Juglandaceae	<i>Artemisia absinthium</i> , <i>Allium sativum</i> , <i>Foeniculum vulgare</i> , <i>Juglans nigra</i> and <i>Stevia rebaudiana</i>	-	Dewormer formula	19 g once daily/3 days (repeated after 62 days)	-	No effect (EPG)	Burke <i>et al.</i> (2009b)
Cucurbitaceae, Asteraceae, Alliaceae, Apiaceae, Lamiaceae	<i>Curcubita pepo</i> , <i>A. vulgaris</i> , <i>A. sativum</i> , <i>F. vulgare</i> , <i>Hyssopus officinalis</i> , <i>Thymus vulgaris</i> , and <i>S. rebaudiana</i>	-	Dewormer formula	19 g dose daily per 7 days	-	No effect (EPG)	Burke <i>et al.</i> (2009b)

Par used: B, Bark; Bu, Bulb; G, Grain; L, Leaf; R, Root; EPG, Eggs per gram; FLC, Faecal Larval Counts; RAW, Reduction Adult Count; PEG, Polyethylene Glycol; DM, Dry Matter; BW, Body Weight; CT, Condensed Tannins

and changes in the anterior part of the digestive tract may interfere with parasite nutrition and consequently lead to malnutrition, reduced fertility and mortality (Martínez-Ortiz-de-Montellano *et al.*, 2013).

The second most found metabolite with anthelmintic activity in goats was the flavonoid. Flavones of the *Turnera ulmifolia* reduced egg hatch, larval development and larval motility of *H. contortus* (Oliveira *et al.*, 2017). Santos *et al.* (2017) have also suggested that flavones (tricin and diosmetin) are related to the anthelmintic activity of *Digitaria insularis*. The extracts of the waste of *Agave sisalana* showed *in vitro* activity on two different stages of the GIN of goats, and their possible active ingredients are flavonoids and saponins (Botura *et al.*, 2013). Thus, saponin is the third class of metabolites most found in plants with anthelmintic activity. Gomes *et al.* (2016) reported this activity of *Zizyphus joazeiro* on eggs of *H. contortus*.

De Medeiros *et al.* (2018) evaluated the *in vitro* effect of water-soluble *Moringa oleifera* lectin (WSMoL) on hatching of eggs and on the development of early-stage larvae of gastrointestinal nematodes from naturally infected goats. The mechanism of action of this substance is attributed to the interference of WSMoL on the activity of proteases and the affinity of the lectin for glycosylated, interacting with intestinal glycoconjugate receptors in the embryo, as well as in cuticle of the larvae.

The extracts rich in sesquiterpene lactones of two forage chicory (*Cichorium intybus*) showed inhibition of hatching of a predominantly *H. contortus* egg population. The most active cultivar presented higher concentration of the 8-deoxylactucin. This action is associated to the presence of  $\alpha$ -methylene- $\gamma$ -lactone functional group capable of reacting with sulfhydryl proteins (Foster *et al.*, 2011).

Two studies have demonstrated the anthelmintic activity of essential oils in goats, obtained from the species *Eucalyptus staigeriana* (Macedo *et al.*, 2010) and *Juniperus pinchotii* (Armstrong *et al.*, 2013). The antiparasitic effect of these plants has been related to the presence of terpenoids (lemonene, eugenol, carvacrol and citral). The chemical substances of this class can act by inhibiting the growth, reducing the reproductive capacity or causing damage during parasite maturation process (Zhu *et al.*, 2013).

Only two studies that used isolated substances of plants were found in this review. Santos *et al.* (2018) used two isolated saponins and presented effect above 90% for egg hatch inhibition (aescin) and larval motility inhibition (digitonin). These authors attributed the anthelmintic effect of saponin to their ability to form complexes with cellular membrane components leading to a pore formation and consequent increase in membrane permeability. The second work was performed by Soldera-Silva *et al.* (2018), who tested quercetin, rutin and epicatechin against *H. contortus* larval. They observed high efficacy with low EC<sub>50</sub> of 7.8, 30 and 10  $\mu\text{g mL}^{-1}$ , respectively.

The therapeutic properties of plants can be attributed to one substance or combination of compounds produced by the secondary metabolism of the plant. Klongsiriwet *et al.* (2015) reported the synergistic effects between the fraction of condensed tannins and two flavonoids, quercetin and luteolin, in terms of inhibiting the *in vitro* exsheathment of *H. contortus* L<sub>3</sub> larvae obtained from small ruminants. The complexity and diversity of structures of the phytocompounds could enable their interaction with multiple molecular targets on the parasite and may consequently hinder the appearance of populations resistant to these substances (Chan-Pérez *et al.*, 2016).

The *in vitro* studies are indicated as screening tests, which must be performed prior to the *in vivo* evaluation. The *in vitro* tests cannot be enough to confirm anthelmintic efficacy of plants, since *in vitro* conditions are different from *in vivo* experiments,

particularly due to the gastrointestinal tract of ruminants. Therefore, pharmacokinetic studies should be carried out for the determination of the natural product bioavailability in small ruminants (Githiori *et al.*, 2006).

### In vivo studies of the anthelmintic activity of plants in goats

The *in vivo* evaluation of the activity of plant against the GIN of goats has been performed mainly by means of FECRT and controlled tests (Githiori *et al.*, 2006). The results obtained in the FECRT cannot estimate anthelmintic efficacy accurately because egg count does not always correlate well with worm numbers. The controlled test is considered as more reliable because the efficacy was measured by the count of adult parasite in the gastrointestinal tract and the evaluation of egg output (Taylor *et al.*, 2002).

The species *Quercus leucotricophora*, *Q. semecarpifolia* and *Desmodium intortum* induced a reduction of EPG, whereas *Bauhinia pulchella* promoted a reduction of egg viability and pasture contamination (Debela *et al.*, 2012; Raju *et al.*, 2015; Lopes *et al.*, 2016). Other plants, such as *A. karroo* and *Lespedeza cuneata*, demonstrated effect against adult parasites (Marume *et al.*, 2012; Gujja *et al.*, 2013). In this review, we observed that some plants, as *A. sisalana*, *A. mearnsii*, *A. nilotica*, were able to promote reduction in the egg count, but did not interfere in the worm burden. The reduction of EPG can be related to a reduction in the nematode burden or a lower fecundity of female worms (Githiori *et al.*, 2006).

There is a lack of specific guidelines for assessing the anthelmintic effect of plant-derived products. The present work identified variations in the protocols applied for *in vivo* studies, especially treatment time, dosage, number of animals, plant preparation and parameters evaluated.

Most of the plants evaluated *in vivo* contain tannin in their chemical composition, and the treatment consisted of the administration of the plant in animal feed. The treatment of goats with leaves of *Bauhinia pulchella* (180 mg kg<sup>-1</sup> per 63 days), rich in condensed tannins, showed reduction in egg viability and pasture contamination of *T. colubriformis* (86%) (Lopes *et al.*, 2016). The administration of the commercial extract of *A. mearnsii* (24 g animal<sup>-1</sup> day<sup>-1</sup>), containing 16.7% of tannins, for an extended period (27 weeks) resulted in the reduction of EPG in the first half of the experimental period. However, there was no effect on the parasite count of adults recovered from goats (Costa-Júnior *et al.*, 2014). The supplementation of goats with sorghum grains, containing high levels of condensed tannins, and the administration of commercial preparation of condensed tannins obtained from the bark of *A. mearnsii* did not significantly influence EPG (Whitley *et al.*, 2009; Max, 2010). According to Costa-Júnior *et al.* (2014), the continuous consumption of tannin may cause an increase in the concentration of salivary proteins, especially in growing animals. These proteins have high affinity for tannin, which can lead to reducing the effect of this active compound.

The addition of *Lespedeza cuneata* hay in the goat diet, in the concentration of 50 to 75%, caused reduction of EPG 84.6 and 91.9%, respectively. Only the treatment with the highest concentration resulted in a significant decrease of the number of adult parasites (74%) (Terrill *et al.*, 2009). In goats, fed pellets with the same species, a significant reduction in the EPG (58 to 70.9%), though there was no reduction in the number of *H. contortus* in the abomasum. The analysis of parasites by electron microscopy revealed changes in the cuticle (constricted folds and a disheveled cuticular surface appearance) (Kommuru *et al.*, 2014, 2015).

Most of the species compiled in this study belong to the family Fabaceae, which presents worldwide distribution. This family includes herbaceous plants, trees and shrubs (perennials or annuals). Some species are used as feed for small ruminants. These plants have agronomic characteristics that could provide beneficial effects to the nutrition and health of animals and environmental issues: palatability for ruminants and nutritive values; biological nitrogen fixation, which reduces the use of chemical fertilizers; carbon sequestration; provision of shade for livestock and flowers for pollinators; conservation of the biodiversity, reduction of methane emission and greenhouse gases (Fagbenro *et al.*, 2015; Hoste *et al.*, 2015). The legume species, *Lespedeza cuneata*, has been widely studied and has shown some advantages as the ability to produce seeds and to be cultivated efficiently, as well as the viability of large-scale production (Hoste *et al.*, 2015). Puchala *et al.* (2005) observed lower methane emissions from goats fed on lespedeza (*Lespedeza cuneata*) and this effect was related to the presence of condensed tannins in the plant.

The use of forage legumes rich in condensed tannins as nutraceutical plants (species that present positive effects for animal nutrition and health) has been proposed to control GIN in small ruminants. Hoste *et al.* (2006) suggested that feeding small ruminants with tannin-rich plants (30–40 g of condensed tannins per kg dry matter) promotes antiparasitic effect. However, the excessive consumption of tannin can cause antinutritional effect in animals. The condensed tannins, at higher concentrations (7–8% DM), can depress feed intake, disturb digestive physiology and decrease nutrient digestibility and the production rate (Min *et al.*, 2003).

Other classes of substances have been associated with anthelmintic activity in goats, such as saponin and essential oils. The treatment of goats naturally infected with gastrointestinal nematodes, with the aqueous extract obtained from the residue *Agave sisalana* (1.7 g kg<sup>-1</sup> per 8 days), led to a reduction of EPG (50.3%) but did not affect the number of adult parasites. This anthelmintic effect was associated with the presence of saponins in this extract (Botura *et al.*, 2011). The oral administration of essential oil obtained from the leaves *E. staigeriana* (500 mg kg<sup>-1</sup>) resulted in a significant reduction of EPG (76.5%) in goats. The chemical constituents present in the oil associated with this activity were the citral and limonene (Macedo *et al.*, 2010).

Differences in anthelmintic efficacy of several plants were verified between the *in vitro* and *in vivo* studies, such as *A. sisalana*, *A. nilotica*, *C. vulgaris* and *L. latisiliquum*, which were more active in *in vitro* assays. The treatment *in vitro* is characterized by direct contact with the parasites and the concentrations of potentially active substances do not always correspond to their *in vivo* bioavailability (Githiori *et al.*, 2006). Furthermore, the possibility of biotransformation of these compounds within the gastrointestinal tract of the animal, modified by rumen microorganism, may lead to a reduction of biological activity (Athanasiadou and Kyriazakis, 2004).

Most studies on potential *in vivo* anti-parasitic plants have showed lower percentage of efficacy to synthetic drugs. An anthelmintic product is considered as effective when it has a percentage reduction of over 90% of EPG and adult parasites (Vercruysee *et al.*, 2001). The treatments with *Vigueira dentata*, *Lespedeza cuneata*, *Elephantorrhiza elephantina*, *Gymnopodium floribundum* and association of *Leucaena leucocephala* and *Mimosa bahamensis* exhibited reduction of EPG over 90%, whereas only one species, *A. karroo*, induced 90% of reduction of adult nematodes (Marume *et al.*, 2012; Maphosa and Masika, 2012b; Gujja *et al.*, 2013; Ventura-Cordero *et al.*, 2017). Githiori *et al.* (2006) suggest that a lower level of reduction should be established (70%) to the evaluation tests *in vivo* herbal preparations, since products with moderate anthelmintic activity may be part of an integrated

program of parasite control in ruminant production systems. The integrated management is the combination of chemical and non-chemical methods of parasite control in order to maintain acceptable levels of production without total elimination of the parasites (Hoste and Torres-Acosta, 2011).

The sustainable control of GIN infection must be guided by three principles: management of grazing systems; stimulation of host response and modulation of worm biology (Hoste *et al.*, 2015). The reduction of contact with infective larvae ( $L_3$ ) can be achieved by strategies of grazing management such as pasture rotation system and mixed grazing. As the  $L_3$  survives on pastures for a limited period of time, the pasture rotation can cut down on the number of parasites ingested by the animal. It has better applicability in tropical climate. Mixed grazing among different animal species or by older animals may also be an alternative for the reduction of  $L_3$  because GIN presents a relative specificity for its hosts. However, mixed grazing between sheep and goats should be avoided due to the strong overlapping of nematodes infecting these two hosts (Torres-Acosta and Hoste, 2008; Hoste and Torres-Acosta, 2011). Another measure for parasite control is the use of organisms that aim at altering the biology of the free-living stages in the environment, decreasing the pasture infectivity. Amongst the various potential agents, one of the most extensively studied models is the use of nematophagous fungi, as *Duddingtonia flagrans*, which has the ability to invade and kill nematode larvae in the faeces (Sanyal *et al.*, 2008).

The stimulation of immune response has been proposed to aid in the control of GIN infection in small ruminants, particularly the genetic selection of resistant animals and the manipulation of host nutrition. This strategy is important for goats since their immune response against GIN is less effective than that observed in sheep. Variability in host response is associated with several factors, such as herbivore behaviors (grazing and/or browsing), age, previous contact with parasites, gender, breed or individual genetic characteristics, nutrition status and the presence of other parasites (Torres-Acosta and Hoste, 2008).

## Conclusions/Future directions

Almost all the plants described in this review showed promising anthelmintic effects, especially *in vitro* studies. However, *in vivo* trials, generally, report lower plant efficacy, probably due to the interference of pharmacokinetic parameters of ruminants in the bioavailability of active compounds of plants. This work also noticed that there is a lack of studies on the effect of chemical constituents isolated from plants against GIN. Condensed tannins were the metabolite class most related with anthelmintic activity, followed by saponins and flavonoids. Studies on the mechanisms of action are required to improve our understanding of interactions between plant secondary metabolites and the different parasitic stages and species. Moreover, efforts should be performed to standardize the formulations of products derived from plants and the validation of their use as anthelmintic in goats. Plants are an important source of new bioactive molecules and may be useful as a part of integrated parasite control, which would lead to the reduction of the use of synthetic anthelmintic drugs.

**Author ORCIDs.**  Mariana Borges Botura, 0000-0002-6404-0314

**Acknowledgements.** We thank teacher Abilio Borghi for the grammar review of the manuscript.

**Financial support.** This study was financed in part by the *Coordenação de Aperfeiçoamento de Pessoal de Nível Superior*–Brasil (CAPES) – Finance Code 001 and *Programa de Pós-graduação em Biotecnologia* of *Universidade Estadual de Feira de Santana* (UEFS).

**Conflict of interest.** The authors declare that they have no conflict of interest.

**Ethical standards.** Not applicable.

## References

- Adamu M, Naidoo V and Eloff JN (2013) Efficacy and toxicity of thirteen plant leaf acetone extracts used in ethnoveterinary medicine in South Africa on egg hatching and larval development of *Haemonchus contortus*. *BMC Veterinary Research* **9**, 01–08.
- Aissa A, Manolaraki F, Ben Salem H, Hoste H and Kraiem K (2016) *In vitro* assessment of the anthelmintic activity of *Hedysarum carnosum* Desf. at different phenological stages and from six locations in Tunisia. *Parasitology* **143**, 778–786.
- Alonso-Díaz MA, Torres-Acosta JFJ, Sandoval-Castro CA, Aguilar-Caballero AJ and Hoste H (2008) *In vitro* larval migration and kinetics of exsheathment of *Haemonchus contortus* larvae exposed to four tropical tanniniferous plant extracts. *Veterinary Parasitology* **153**, 313–319.
- Alonso-Díaz MA, Torres-Acosta JFJ, Sandoval-Castro CA and Hoste H (2011) Comparing the sensitivity of two *in vitro* assays to evaluate the anthelmintic activity of tropical tannin rich plant extracts against *Haemonchus contortus*. *Veterinary Parasitology* **181**, 360–364.
- Al-Rofaai A, Rahman WA, Sulaiman SF and Yahaya ZS (2012a) *In vitro* ovicidal and larvicidal activity of methanolic leaf extract of *Manihot esculenta* (cassava) on susceptible and resistant strains of *Trichostrongylus colubriformis*. *Veterinary Parasitology* **190**, 127–135.
- Al-Rofaai A, Rahman WA, Sulaiman SF and Yahaya ZS (2012b) *In vitro* activity of neem (*Azadirachta indica*) and cassava (*Manihot esculenta*) on three pre-parasitic stages of susceptible and resistant strains of *Teladorsagia (ostertagia) circumcincta*. *Veterinary Parasitology* **188**, 85–92.
- Andre WPP, Ribeiro WLC, Cavalcante GS, Santos JML, Macedo ITF, de Paula HCB, Freitas RM, Morais SM, Melo JV and Bevilacqua CML (2016) Comparative efficacy and toxic effects of carvacryl acetate and carvacrol on sheep gastrointestinal nematodes and mice. *Veterinary Parasitology* **218**, 52–58.
- Armstrong SA, Klein DR, Whitney TR, Scott CB, Muir JP, Lambert BD and Craig TM (2013) Effect of using redberry juniper (*Juniperus pinchotii*) to reduce *Haemonchus contortus* *in vitro* motility and increase ivermectin efficacy. *Veterinary Parasitology* **197**, 271–276.
- Athanasiadou S and Kyriazakis I (2004) Plant secondary metabolites: anti-parasitic effects and their role in ruminant production systems. *Proceedings of the Nutrition Society* **63**, 631–639.
- Azaizeh H, Halahleh F, Abbas N, Markovics A, Muklada H, Ungar ED and Landau SY (2013) Polyphenols from *Pistacia lentiscus* and *Phillyrea latifolia* impair the exsheathment of gastro-intestinal nematode larvae. *Veterinary Parasitology* **191**, 44–50.
- Azaizeh H, Mrenya R, Markovics A, Muklada H, Glazer I and Landau SY (2015) Seasonal variation in the effects of Mediterranean plant extracts on the exsheathment kinetics of goat gastrointestinal nematode larvae. *Small Ruminant Research* **131**, 130–135.
- Bentounsi B, Meradi S and Cabaret J (2012) Towards finding effective indicators (diarrhoea and anaemia scores and weight gains) for the implementation of targeted selective treatment against the gastro-intestinal nematodes in lambs in a steppe environment. *Veterinary Parasitology* **187**, 275–279.
- Borges DGL and Borges FDA (2016) Plants and their medicinal potential for controlling gastrointestinal nematodes in ruminants. *Nematoda* **3**, 1–7.
- Botura MB, Silva GD, Lima HG, Oliveira JVA, Souza TS, Santos JDG, Branco A, Moreira ELT, Almeida MAO and Batatinha MJM (2011) *In vivo* anthelmintic activity of an aqueous extract from sisal waste (*Agave sisalana* Perr.) against gastrointestinal nematodes in goats. *Veterinary Parasitology* **177**, 104–110.
- Botura MB, Santos JDG, Silva GD, Lima HG, Oliveira JVA, Almeida MAO, Batatinha MJM and Branco A (2013) *In vitro* ovicidal and larvicidal activity of *Agave sisalana* Perr. (sisal) on gastrointestinal nematodes of goats. *Veterinary Parasitology* **192**, 211–217.
- Brito DRB, Costa-Júnior LM, Garcia JL, Torres-Acosta JFJ, Louvandini H, Cutrim-Júnior JAA, Araújo JEM and Soares EDS (2018) Supplementation with dry *Mimosa caesalpiniiifolia* leaves can reduce the *Haemonchus contortus* worm burden of goats. *Veterinary Parasitology* **252**, 47–51.
- Brunet S, Jackson F and Hoste H (2008a) Effects of sainfoin (*Onobrychis viciifolia*) extract and monomers of condensed tannins on the association

- of abomasal nematode larvae with fundic explants. *International Journal for Parasitology* **38**, 783–790.
- Brunet S, Martínez-Ortiz de Montellano C, Torres-Acosta JFJ, Sandoval-Castro CA, Aguilar-Caballero AJ, Capetillo-Leal C and Hoste H** (2008b) Effect of the consumption of *Lysiloma latisiliquum* on the larval establishment of gastrointestinal nematodes in goats. *Veterinary Parasitology* **157**, 81–88.
- Brunet S, Fourquaux I and Hoste H** (2011) Ultrastructural changes in the third-stage, infective larvae of ruminant nematodes treated with sainfoin (*Onobrychis viciifolia*) extract. *Parasitology International* **60**, 419–424.
- Burke JM, Wells A, Casey P and Kaplan RM** (2009a) Garlic and papaya lack control over gastrointestinal nematodes in goats and lambs. *Veterinary Parasitology* **159**, 171–174.
- Burke JM, Wells A, Casey P and Kaplan RM** (2009b) Herbal dewormer fails to control gastrointestinal nematodes in goats. *Veterinary Parasitology* **160**, 168–170.
- Cabardo Jr DE and Portugaliza HP** (2017) Anthelmintic activity of *Moringa oleifera* seed aqueous and ethanolic extracts against *Haemonchus contortus* eggs and third stage larvae. *International Journal of Veterinary Science and Medicine* **5**, 30–34.
- Cantacessi C, Campbell BE and Gasser RB** (2012) Key strongylid nematodes of animals – Impact of next-generation transcriptomics on systems biology and biotechnology. *Biotechnology Advances* **30**, 469–488.
- Celaya R, Ferreira LMM, Moreno-Gonzalo J, Frutos P, Hervás G, Ferre I, García U, Ortega-Mora LM and Osoro K** (2010) Effects of heather and oat supplementation on gastrointestinal nematode infections and performance of grazing Cashmere goats. *Small Ruminant Research* **91**, 186–192.
- Chan-Pérez JI, Torres-Acosta JFJ, Sandoval-Castro CA, Hoste H, Castañeda-Ramírez GS, Vilarem G and Mathieu C** (2016) *In vitro* susceptibility of ten *Haemonchus contortus* isolates from different geographical origins towards acetone: water extracts of two tannin rich plants. *Veterinary Parasitology* **217**, 53–60.
- Costa-Júnior LM, Costa JS, Lôbo ICPD, Soares AMS, Abdala AL, Chaves DP, Batista ZS and Louvandini H** (2014) Long-term effects of drenches with condensed tannins from *Acacia mearnsii* on goats naturally infected with gastrointestinal nematodes. *Veterinary Parasitology* **205**, 725–729.
- Debela E, Tolera A, Eik LO and Salte R** (2012) Condensed tannins from *Sesbania sesban* and *Desmodium intortum* as a means of *Haemonchus contortus* control in goats. *Tropical Animals Health and Production* **44**, 1939–1944.
- De Medeiros MLS, de Moura MC, Napoleão TH, Paiva PMG, Coelho LCBB, Bezerra ACDS and da Silva MDC** (2018) Nematicidal activity of a water soluble lectin from seeds of *Moringa oleifera*. *International Journal of Biological Macromolecules* **108**, 782–789.
- Domingues LF, Botura MB, Da Cruz ACFG, Yuki CC, Da Silva GD, Costa S, Murphy G, Moreira ELT, De Meneses IDS, De Almeida MGAR, Branco A, De Almeida MAO and Batatinha MJM** (2010) Evaluation of anthelmintic activity of liquid waste of *Agave sisalana* (sisal) in goats. *Revista Brasileira de Parasitologia Veterinária* **19**, 270–272.
- Fagbenro JA, Oshunsanya SO, Aluko PA and Oyeleye BA** (2015) Biomass production, tissue nutrient concentration, and N2-Fixing potentials of seven tropical leguminous species. *Communications in Soil Science and Plant Analysis* **46**, 709–723.
- Foster IG, Cassida KA and Turner KE** (2011) *In vitro* analysis of anthelmintic activity of forage chicory (*Cichorium intybus* L.) sesquiterpene lactones against a predominantly *Haemonchus contortus* egg population. *Veterinary Parasitology* **180**, 298–306.
- Gárate-Gallardo L, de Torres-Acosta JFJ, Aguilar-Caballero AJ, Sandoval-Castro CA, Cámara-Sarmiento R and Canul-Ku HL** (2015) Comparing different maize supplementation strategies to improve resilience and resistance against gastrointestinal nematode infections in browsing goats. *Parasite* **22**, 1–9.
- Githiori JB, Athanasiadou S and Thamsborg SM** (2006) Use of plants in novel approaches for control of gastrointestinal helminths in livestock with emphasis on small ruminants. *Veterinary Parasitology* **139**, 308–320.
- Gomes DC, Lima HG, Vaz AV, Santos NS, Santos FO, Dias ER, Botura MB, Branco A and Batatinha MJM** (2016) *In vitro* anthelmintic activity of the *Zizyphus joazeiro* bark against gastrointestinal nematodes of goats and its cytotoxicity on Vero cells. *Veterinary Parasitology* **226**, 10–16.
- Gujja S, Terrill TH, Mosjidis JA, Miller JE, Mechineni A, Kommuru DS, Shaik SA, Lambert BD, Cherry NM and Burke JM** (2013) Effect of supplemental *sericea lespedeza* leaf meal pellets on gastrointestinal nematode infection in grazing goats. *Veterinary Parasitology* **191**, 51–58.
- Hernández-Vilegas MM, Borges-Argáez R, Rodríguez-Vivas RI, Torres-Acosta JFJ, Méndez-González M and Cáceres-Farfán M** (2011) Ovicidal and larvicidal activity of the crude extracts from *Phytolacca icosandra* against *Haemonchus contortus*. *Veterinary Parasitology* **179**, 100–106.
- Hernández-Vilegas MM, Borges-Argáez R, Rodríguez-Vivas RI, Torres-Acosta JFJ, Méndez-González M and Cáceres-Farfán M** (2012) *In vivo* anthelmintic activity of *Phytolacca icosandra* against *Haemonchus contortus* in goats. *Veterinary Parasitology* **189**, 284–290.
- Hoste H, Athanasiadou S, Thamsborg SM and Hoskin SO** (2006) The effects of tannin-rich plants on parasitic nematodes in ruminants. *Trends in Parasitology* **22**, 253–261.
- Hoste H, Sotiraki S, Landau SY, Jackson F and Beveridge I** (2010) Goat-nematode interactions: think differently. *Trends in Parasitology* **26**, 376–381.
- Hoste H and Torres-Acosta JFJ** (2011) Non chemical control of helminths in ruminants: adapting solutions for changing worms in a changing world. *Veterinary Parasitology* **180**, 144–154.
- Hoste H, Torres-Acosta JFJ, Sandoval-Castro CA, Mueller-Harvey I, Sotiraki S, Louvandini H, Thamsborg SM and Terrill TH** (2015) Tannin containing legumes as a model for nutraceuticals against digestive parasites in livestock. *Veterinary Parasitology* **212**, 5–17.
- Houngzangbe-Adote MS, Paolini V, Fouraste I, Moutairou K and Hoste H** (2005) *In vitro* effects of four tropical plants on three life-cycle stages of the parasitic nematode, *Haemonchus contortus*. *Research in Veterinary Science* **78**, 155–160.
- Jamous RM, Ali-Shtayeh MS, Abu-Zaitoun SY, Markovics A and Azaizeh H** (2017) Effects of selected Palestinian plants on the *in vitro* exsheathment of the third stage larvae of gastrointestinal nematodes. *BMC Veterinary Research* **13**, 1–11.
- Kaminsky R, Bapst B, Stein PA, Strehlau GA, Allan BA, Hosking BC, Rolfe PF and Sager H** (2011) Differences in efficacy of monepantel, derquantel and abamectin against multi-resistant nematodes of sheep. *Parasitology Research* **109**, 19–23.
- Klongsiriwet C, Quijada J, Williams AR, Mueller-Harvey I, Williamson EM and Hoste H** (2015) Synergistic inhibition of *Haemonchus contortus* exsheathment by flavonoid monomers and condensed tannins. *International Journal for Parasitology: Drugs and Drug Resistance* **5**, 127–134.
- Kommuru DS, Barker T, Desai S, Burke JM, Ramsay A, Mueller-Harvey I, Miller JE, Mosjidis JA, Kamiseti N and Terrill TH** (2014) Use of pelleted *Sericea lespedeza* (*Lespedeza cuneata*) for natural control of coccidia and gastrointestinal nematodes in weaned goats. *Veterinary Parasitology* **204**, 191–198.
- Kommuru DS, Whitley NC, Miller JE, Mosjidis JA, Burke JM, Gujja S, Mechineni A and Terrill TH** (2015) Effect of *Sericea lespedeza* leaf meal pellets on adult female *Haemonchus contortus* in goats. *Veterinary Parasitology* **207**, 170–175.
- Landau S, Azaizeh H, Muklada H, Glasser T, Ungar ED, Baram H, Abbas N and Markovics A** (2010) Anthelmintic activity of *Pistacia lentiscus* foliage in two Middle Eastern breeds of goats differing in their propensity to consume tannin-rich browse. *Veterinary Parasitology* **173**, 280–286.
- Lima HG, Gomes DC, Santos NS, Dias ER, Botura MB, Batatinha MJM and Branco A** (2017) *Prosopis juliflora* pods alkaloid-rich fraction: *In vitro* anthelmintic activity on goat gastrointestinal parasites and its cytotoxicity on vero cells. *Pharmacognosy Magazine* **13**(suppl. 3), S684.
- Lopes SG, Barros LB, Louvandini H, Abdalla AL and Junior LMC** (2016) Effect of tanniniferous food from *Bauhinia pulchella* on pasture contamination with gastrointestinal nematodes from goats. *Parasites & Vectors* **9**, 102.
- Macedo ITE, Bevilaqua CML, Oliveira LMB, Camurça-Vasconcelos ALF, Vieira LS, Oliveira FR, Queiroz-Junior EM, Tomé AR and Nascimento NRF** (2010) Anthelmintic effect of *Eucalyptus staigeriana* essential oil against goat gastrointestinal nematodes. *Veterinary Parasitology* **173**, 93–98.
- Maphosa V and Masika PJ** (2012a) *In vivo* validation of *Aloe ferox* (Mill). *Elephantorrhiza elephantina* Bruch. Skeels. and *Leonotis leonurus* (L) R. BR as potential anthelmintics and antiprotozoals against mixed infections of gastrointestinal nematodes in goats. *Parasitology Research* **110**, 103–108.
- Maphosa V and Masika PJ** (2012b) The potential of *Elephantorrhiza elephantina* as an anthelmintic in goats. *Parasitology Research* **111**, 881–888.

- Martínez-Ortiz-de-Montellano C, Arroyo-López C, Fourquaux I, Torres-Acosta JFJ, Sandoval-Castro CA and Hoste H (2013) Scanning electron microscopy of *Haemonchus contortus* exposed to tannin-rich plants under *in vivo* and *in vitro* conditions. *Experimental Parasitology* **133**, 281–286.
- Marume U, Chimonyo M and Dzama K (2012) Influence of dietary supplementation with *Acacia karroo* on experimental haemonchosis in indigenous Xhosa lop-eared goats of South Africa. *Livestock Science* **144**, 132–139.
- Max RA (2010) Effect of repeated wattle tannin drenches on worm burdens, faecal egg counts and egg hatchability during naturally acquired nematode infections in sheep and goats. *Veterinary Parasitology* **169**, 138–143.
- Mechineni A, Kommuru DS, Gujja S, Mosjidis JA, Miller JE, Burke JM, Ramsay A, Mueller-Harvey I, Kannan G, Lee JH, Kouakou B and Terrill TH (2014) Effect of fall-grazed sericea lespedeza (*Lespedeza cuneata*) on gastrointestinal nematode infections of growing goats. *Veterinary Parasitology* **204**, 221–228.
- Min BR, Barry TN, Attwood GT and McNabb WC (2003) The effect of condensed tannins on the nutrition and health of ruminants fed fresh temperate forages: a review. *Animal Feed Science and Technology* **106**, 3–19.
- Molento MB, Fortes F, Pondelek D, Borges F, Chagas AC, Torres-Acosta JF and Geldhof P (2011) Challenges of nematode control in ruminants: focus on Latin America. *Veterinary Parasitology* **180**, 126–132.
- Moreno FC, Gordon IJ, Knox MR, Summer PM, Skerrat LF, Benvenuti MA and Saumell CA (2012) Anthelmintic efficacy of five tropical native Australian plants against *Haemonchus contortus* and *Trichostrongylus colubriformis* in experimentally infected goats (*Capra hircus*). *Veterinary Parasitology* **187**, 237–243.
- Moreno-Gonzalo J, Manolaraki F, Frutos P, Hervás G, Celaya R, Osoro K, Ortega-Mora LM, Hoste H and Ferre I (2013a) *In vitro* effect of heather (Ericaceae) extracts on different development stages of *Teladorsagia circumcincta* and *Haemonchus contortus*. *Veterinary Parasitology* **197**, 235–243.
- Moreno-Gonzalo J, Manolaraki F, Frutos P, Hervás G, Celaya R, Osoro K, Ortega-Mora LM, Hoste H and Ferre I (2013b) *In vitro* effect of heather extracts on *Trichostrongylus colubriformis* eggs, larvae and adults. *Veterinary Parasitology* **197**, 586–594.
- Moreno-Gonzalo J, Osoro K, García U, Frutos P, Celaya R, Ferreira LMM, Ortega-Mora LM and Ferre I (2013c) Effect of the consumption of heather on incoming larvae and established population of *Teladorsagia circumcincta* in experimentally infected Cashmere goats. *Veterinary Parasitology* **196**, 124–129.
- Moreno-Gonzalo J, Osoro K, García U, Frutos P, Celaya R, Ferreira LMM, Ortega-Mora LM and Ferre I (2014) Anthelmintic effect of heather in goats experimentally infected with *Trichostrongylus colubriformis*. *Parasitology Research* **113**, 693–699.
- Naumann HD, Armstrong SA, Lambert BD, Muir JP, Tedeschi LO and Kothmann MM (2014) Effect of molecular weight and concentration of legume condensed tannins on *in vitro* larval migration inhibition of *Haemonchus contortus*. *Veterinary Parasitology* **199**, 93–98.
- O'Grady J and Kotze AC (2004) *Haemonchus contortus*: *in vitro* drug screening assays with the adult life stage. *Experimental Parasitology* **106**, 164–172.
- Oliveira AF, Junior LMC, Lima AS, Silva CR, Ribeiro MN, Mesquita JW, Rocha CQ, Tangerina MM and Vilegas W (2017) Anthelmintic activity of plant extracts from Brazilian savanna. *Veterinary Parasitology* **236**, 121–127.
- Osoro K, Celaya R, Moreno-Gonzalo J, Ferreira LMM, García U, Frutos P, Ortega-Mora LM and Ferre I (2009) Effects of stocking rate and heather supplementation on gastrointestinal nematode infections and host performance in naturally-infected cashmere goats. *Rangeland Ecology & Management* **62**, 127–135.
- Preet S and Tomar RS (2017) Anthelmintic effect of biofabricated silver nanoparticles using *Ziziphys jujuba* leaf extract on nutritional status of *Haemonchus contortus*. *Small Ruminant Research* **154**, 45–51.
- Puchala R, Min BR, Goetsch AL and Sahl T (2005) The effect of a condensed tannin-containing forage on methane emission by goats. *Journal of Animal Science* **83**, 182–186.
- Raju J, Sahoo B, Chandrakar A, Sankar M, Garg AK, Sharma AK and Pandey AB (2015) Effect of feeding oak leaves (*Quercus semecarpifolia* vs *Quercus leucotricophora*) on nutrient utilization, growth performance and gastrointestinal nematodes of goats in temperate sub Himalayas. *Small Ruminant Research* **125**, 1–9.
- Roeber F, Jex AR and Gasser RB (2013) Impact of gastrointestinal parasitic nematodes of sheep, and the role of advanced molecular tools for exploring epidemiology and drug resistance – an Australian perspective. *Parasites & Vectors* **6**, 153.
- Santos FO, Lima HG, Santos NSS, Serra TM, Uzeda RSU, Reis IMA, Botura MB, Branco A and Batatinha MJM (2017) *In vitro* anthelmintic and cytotoxicity activities of the *Digitaria insularis* (Poaceae). *Veterinary Parasitology* **245**, 48–54.
- Santos ACV, Santos FO, Lima HG, Da Silva GD, Uzêda RS, Dias ÊR, Branco A, Cardoso KV, David JM, Botura MB, Costa SL and Batatinha MJM (2018) *In vitro* ovicidal and larvicidal activities of some saponins and flavonoids against parasitic nematodes of goats. *Parasitology* **145**, 1884–1889.
- Sanyal PK, Sarkar AK, Patel NK, Mandal SC and Pal S (2008) Formulation of a strategy for the application of *Duddingtonia flagrans* to control caprine parasitic gastroenteritis. *Journal of Helminthology* **82**, 169–174.
- Silveira RX, Chagas ACS, Botura MB, Batatinha MJM, Katiki LM, Carvalho CO, Bevilacqua CML, Branco A, Machado EAA, Borges SL and Almeida MA (2012) Action of sisal (*Agave sisalana*, Perrine) extract in the *in vitro* development of sheep and goat gastrointestinal nematodes. *Experimental Parasitology* **131**, 162–168.
- Sokerya S, Waller PJ, Try P and Höglund J (2009) The effect of long-term feeding of fresh and ensiled cassava (*Manihot esculenta*) foliage on gastrointestinal nematode infections in goats. *Tropical Animal Health and Production* **41**, 251–258.
- Soldera-Silva A, Seyfried M, Campestrini LH, Zawadzki-Baggio SF, Minho AP, Molento MB and Maurer JBB (2018) Assessment of anthelmintic activity and bio-guided chemical analysis of *Persea americana* seed extracts. *Veterinary Parasitology* **251**, 34–43.
- Taylor MA, Hunt KR and Goodyear KL (2002) Anthelmintic resistance detection methods. *Veterinary Parasitology* **103**, 183–194.
- Terrill TH, Dykes GS, Shaik SA, Miller JE, Kouakou B, Kannan G, Burke JM and Mosjidis JA (2009) Efficacy of *Sericea lespedeza* hay as a natural dewormer in goats: dose titration study. *Veterinary Parasitology* **163**, 52–56.
- Torina A, Dara S, Marino AMF, Sparagano OAE, Vitale F, Reale S and Caracappa S (2004) Study of gastrointestinal nematodes in Sicilian sheep and goats. *Annals of the New York Academy of Sciences* **1026**, 187–194.
- Torres-Acosta JFJ and Hoste H (2008) Alternative or improved methods to limit gastro-intestinal parasitism in grazing sheep and goats. *Small Ruminant Research* **77**, 159–173.
- Torres-Acosta JFJ, Jacobs DE, Aguilar-Caballero A, Sandoval-Castro C, May-Martinez M and Cob-Galera LA (2004) The effect of supplementary feeding on the resilience and resistance of browsing Criollo kids against natural gastrointestinal nematode infections during the rainy season in tropical Mexico. *Veterinary Parasitology* **124**, 217–238.
- Vercruyse J, Holdsworth P, Letonja T, Barth D, Conder G, Hamamoto K and Okano K (2001) International harmonisation of anthelmintic efficacy guidelines. *Veterinary Parasitology* **96**, 171–193.
- Ventura-Cordero J, González-Pech PG, Jaimez-Rodríguez PR, Ortiz-Ocampo GI, Sandoval-Castro CA and Torres-Acosta JFJ (2017) Gastrointestinal nematode infection does not affect selection of tropical foliage by goats in a cafeteria trial. *Tropical Animal Health and Production* **49**, 97–104.
- Whitley NC, Miller JE, Burke JM, Cazac D, O'Brien DJ, Dykes L and Muir JP (2009) Effect of high tannin grain sorghum on gastrointestinal parasite fecal egg counts in goats. *Small Ruminant Research* **87**, 105–107.
- Zabré G, Kaboré A, Bayala B, Katiki LM, Costa-Júnior LM, Tamboura HH, Belem AMG, Abdalla AL, Niderkorn V, Hoste H and Louvandini H (2017) Comparison of the *in vitro* anthelmintic effects of *Acacia nilotica* and *Acacia raddiana*. *Parasite* **44**, 1–11.
- Zhu L, Dai J, Yang L and Qiu J (2013) Anthelmintic activity of *Arisaema franchetianum* and *Arisaema lobatum* essential oils against *Haemonchus contortus*. *Journal of Ethnopharmacology* **148**, 311–316.