Journal MVZ Cordoba
2021; september-december. 26(3):e2317.
https://doi.org/10.21897/rmvz.2317

Original

In vivo anthelmintic activity of terpenes and essential oils in small ruminants

Rafael Arturo Torres-Fajardo[1*]; Rosa Isabel Higuera-Piedrahita[2]

[1] Universidad Autónoma de Yucatán, Facultad de Medicina Veterinaria y Zootecnia, Yucatán, México
[2]Universidad Nacional Autónoma de México. Facultad de Estudios Superiores Cuautitlán. Cuautitlán. México
*Correspondence: rafael-arturo-torres@outlook.es

Received: March 2021; Accepted: June 2021; Published: June 2021.

ABSTRACT

Terpenes and essential oils (EsOi) have a wide range of biological activities that could be explored in veterinary sciences. In this sense, their use has been proposed as a strategy to overcome the growing populations of gastrointestinal nematodes (GIN) resistant to the traditional anthelmintic (AH) drugs. In the present review, we analysed eleven scientific manuscripts aimed to evaluate the AH activity of terpene-rich plants (TRP) and EsOi in small ruminants by using the *in vivo* approach. The sheep species was used in the 81% of works. Brazil is the country leading this research line, followed by the United States of America and Benin. All the analysed manuscripts employed the faecal egg count reduction test, while five manuscripts employed the controlled test —or trial— methodology. The activity of TRP and EsOi on the faecal excretion of GIN eggs was variable, showing values between zero to 97%. Two manuscripts reported a reduction in the size of male GIN, as well as the fecundity of female GIN after administration of EsOi. It would be worth to perform more works aimed to understand the relationships between plants, their secondary metabolites and the ruminants consuming them. Through the understanding of such interactions, we will be allowed to use these natural products as elements that could contribute to improve the nutrition and health of sheep and goats under different productive systems.

Keywords: Ethnoveterinary; gastrointestinal nematodes; goat; parasite egg count; parasitic diseases; plant secondary metabolites; sheep (*Sources: CAB, MeSH*)

RESUMEN

Los terpenos y aceites esenciales (AcEs) poseen un amplio espectro de actividades biológicas que pueden ser exploradas en las ciencias veterinarias. En este sentido, su uso ha sido propuesto como una estrategia para enfrentar las crecientes poblaciones de nematodos gastrointestinales (NGI) resistentes a los antihelmínticos (AH) tradicionales. En la presente revisión analizamos 11 manuscritos científicos que, mediante la utilización del enfoque *in vivo*, evaluaron el potencial AH de plantas ricas en terpenos (PRT) o AcEs en pequeños rumiantes. La especie ovina fue utilizada en el 81% de los trabajos. Brasil es el país que lidera esta línea de investigación seguido de los Estados Unidos de América y la República de Benín. Todos los manuscritos analizados utilizaron la prueba de reducción

How to cite (Vancouver).
Torres-Fajardo RA, Higuera-Piedrahita RI. *In vivo* anthelmintic activity of terpenes and essential oils in small ruminants. Rev MVZ Cordoba. 2021; 26(3):e2317. https://doi.org/10.21897/rmvz.2317

del conteo fecal de huevos de NGI, mientras que cinco manuscritos emplearon la metodología del test —o prueba— controlado(a). La actividad de las PRT y los AcEs sobre la excreción de huevos de NGI en las heces fue variable, reportándose valores que oscilaron desde un efecto nulo hasta un 97%. Dos trabajos reportaron una reducción en el tamaño de los NGI machos adultos y en la fecundidad de las hembras tras la administración de AcEs. Resulta necesario generar más trabajos que se dirijan a entender las interacciones entre las plantas, sus metabolitos secundarios y los rumiantes que las consumen. Comprender dichas interacciones nos permitirá utilizar estos productos naturales como elementos que ayuden a mejorar la nutrición y la sanidad de ovinos y caprinos en diferentes sistemas productivos.

Palabras clave: Conteo de huevos de parásitos; enfermedades parasitarias; etnoveterinaria; nematodos gastrointestinales; cabras; metabolitos secundarios de plantas; ovejas (*Fuentes: CAB, MeSH*).

INTRODUCTION

Integrated control of gastrointestinal nematodes in small ruminants

Any sheep/goat livestock system based on pasture utilization has the unavoidable consequence of face gastrointestinal nematodes (GIN). Nowadays, the infection caused by GIN continues to be considered as the main health drawback for small ruminant flocks, which negatively impairs the viability and profitability of these livestock systems (1,2). The latter situation is worsened with the triggering of GIN strains resistant to traditional anthelmintics (AH), even toward the recently introduced active principles (5-8). According with some estimates, losses associated with GIN infection are —in average— 151,206, and 86 million euros in dairy sheep, meat sheep, and dairy goat industries, respectively (9). Likewise, the European Union reported losses averaging 1.8 billion euros associated with AH resistance (10). In the search for non-pharmacological and sustainable strategies, the concept of '*integrated control of gastrointestinal nematodes'* has been embedded. This compendium of strategies is inherently complementary (allowing the possibility for combinations at the farm level) and is aimed to favor the control over GIN eradication. Within this range of possibilities, it is worth to mention the rational use of AH (11,12), nutritional supplementation (13,14), genetic selection (15,16), immunization (17,18), copper oxide wire particles (19,20), rotational grazing (21), bio control (22,23), and the elucidation of AH properties in many plant species (24,25,26).

Plant secondary metabolites and their anthelmintic potential

Without any exception, all plant species produce different quantities and concentrations of certain elements that possess various biological functions documented to date. These elements have been received plenty of labels (27) such as *antinutritional factors*, *plant secondary compounds*, *specialized metabolites*, and *plant secondary metabolites* (PSM). The PSM are highly specialized chemical compounds produced by plants through different metabolic pathways derived from the primary metabolism (28). Yet, their presence is influenced by environmental stressful conditions, which has been named *plant epigenetic* (29). The PSM production is affected by the plant exposition to light, temperature, stress, and specific soil characteristics such as pH and salinity (30,31).

The traditional view in animal and veterinary sciences has tagged the PSM as substances produced with the purpose to avoid herbivory (32). Nonetheless, from an ecological perspective, their production represents specific adaptations improving the resilience, plasticity, and interaction of plants with their environment (33,34). Furthermore, it is necessary to consider that the term *herbivore* comprises different animal classes such as insects, which have coexisted with PSM for 350 million years (35), or orders such as ruminants, whose families entered into the ecosystem chronology some 18-23 million years (36). Therefore, relationships between animals and PSM are represented by a mutual adaptive response. Consequently, the PSM intake could represent health benefits derived from many mechanisms. These include the bioactive properties against different GIN species (24,25,26). Currently, there are 200,000 PSM (37), albeit this number could represent an under-estimation (38). Because of their heterogeneous chemical composition, many classification systems exist, however, we can divide PSM at follows:

i.) Alkaloids: Which represent the formal beginning of PSM research when the German pharmacist Friedrich Sertürner isolated morphin in 1806 (32). This family possess 20,000 structures identified to date (39) and their AH properties have been a current research avenue (40,41).

ii.) Phenolic compounds: Which have 8,000 identified structures (42) and represent the most studied PSM family in relation with the bioactive properties against small ruminants' GIN. Within this group, the condensed tannins have been received special attention due to their presence in many plants from native vegetation systems worldwide (43,44,45).

iii.) Terpenes: Which represents the largest and highly complex group with some 80,000 identified structures to date (46) and whose AH activity is the aim of the present revision.

Terpenes, terpenoids and isoprenoids

From a structural and chemical perspective, these PSM belong to the most diverse and complex group. The steroids and carotenoids also belong to this PSM family. Currently, a third part of the natural product dictionary (http://dnp.chemnetbase.com) belongs to the so-called '*terpenome'*. This PSM group is characterized by a remarkable diversity, whose basic structure follows the principle of isoprene units (C_5)n, also known as 2-methyl-butane. Depending on the sub-unities (n) number they are classified as hemiterpenes (C_5), monoterpenes (C_{10}), sesquiterpenes (C_{15}), diterpenes (C_{20}), sesterterpenes (C_{25}), triterpenes (C_{30}), and tetraterpenes (C_{40}) (47). Broadly, terpenes are volatile compounds responsible for the odor in many plant species and fruits. The term "*terpene*" is derived from a volatile oil (*turpentine*) obtained from some pine tree species (48). Because their ample distribution within the vegetal kingdom, these PSM could be present in a plethora of botanic families such as Apiaceae, Asteraceae, Euphorbiaceae, Fabaceae, Lamiaceae, Myrtaceae, Poaceae, Rutaceae, Verbenaceae, among many other. In addition, they are synthetized by insects and marine organisms (49). Another important reminder is that, in contrast to terpenes, terpenoids have a structural added group to its chemical composition.

Terpenes are highly lipophilic and volatiles into the environment, constituting a big proportion of the plant organic volatile compounds (OVC). The main constituents of OVC are the monoterpenes and sesquiterpenes, followed by compounds with aromatic rings, fatty acids, and volatile amino acids (50). In contrast, diterpenes and triterpenes are less volatile. OVC are used by fruits and flowers to send signals at some animals, mainly insects (51). In addition, there are reports suggesting that herbivory elicits monoterpenes and some sesquiterpenes in OVC form (48).

The rising interest on terpenes and OVC has triggered the development of methodologies allowing to obtain, isolate, or purify such classes of PSM. These methodologies based —at their majority— on chemical processes have allowed the isolation and characterization of some secondary metabolites. In this sense, the essential oils (EsOi) synthesis represents an alternative to obtain PSM combinations widely used in the animal, pharmaceutical, agricultural, and cosmetic industries, among others.

Essential oils

Define with preciseness the EsOi is not an easy task, given the heterogeneity in their chemical composition and the myriad of properties which have been attributed to them in many human activities such as the pharmaceutical, cosmetic, veterinary, and livestock industries. The table 1 shows some literature concepts about EsOi. Nonetheless, some considerations should be highlighted in order to clarify this concept. Apart from its name, EsOi are not truly oils (lipids). In the same way, the term '*essential'*, does not refer to a like-determinant property, but to their relations with some components responsible for the fragrance or *quinta essentia* in plants (52), thus, its name is derived from the word '*essence'*. EsOi could be obtained from many plant structures (leaves, flowers, stems, fruits, pods, seeds, roots, and barks) or even marine organisms, and represent lipophilic mixtures that contain a variety of chemical compounds (between 20 to 60) obtained by many methodologies (53). Therefore, we might consider the EsOi as oily substances containing different classes of PSM, within which monoterpenes and sesquiterpenes constitute a high proportion. Finally, it is noteworthy to consider that although their bioactive effects could be attributed to their mainly components, synergies between PSM have to be considered and studied.

Table 1. The essential oils concept according to some authors.

Definition	Reference
Mixtures of secondary metabolites obtained by the plant volatile fraction through steam distillation	(54)
Highly volatile aromatic compounds extracted from plants by steam or solvent distillation	(55)
Complex mixtures of bioactive compounds which possess volatile, lipophilic, odoriferous, and liquid substances	(56)
Volatile and hydrophobic liquids extracted from plants, generally rich in aromas	(57)
Highly heterogeneous, aromatic, and volatile mixtures of secondary metabolites	(58)

Considering the need for non-pharmacological strategies aimed to face the GIN and the resistance toward commercial therapeutic products, the AH properties of both terpenes (59,60) and EsOi (61) have been documented. Therefore, the review presented here, represents an effort to compile the outcomes of some scientific manuscripts which evaluated the AH activity of terpenes and EsOi in small ruminants under an *in vivo* approach. In addition, we will discuss their applicability and some knowledge gaps deserving more investigation in the future. We include manuscripts submitted to peer-reviewed journals and published during the last two decades (2001-2021). The inclusion methods were established under the following criteria: (i) manuscripts employing the *in vivo* approach, (ii) manuscripts focusing on sheep and/or goats, (iii) manuscripts related with a patent GIN infection, (iv) manuscripts using terpene-rich plants or EsOi and, (v) manuscripts associating the intake of terpene-rich plants or EsOi with the GIN infection.

After the search and manuscript selection process, we recovered 11 works fulfilling the inclusion criteria. Table 2 shows some methodological aspects in the analyzed manuscripts. Brazil, with seven works, is the country that leads this research line, followed by three manuscripts performed in the United States of America, and one work executed in the republic of Benin. All manuscripts used the fecal egg count reduction test (FECRT), whereas five employed the controlled test (CnT). The 81% (9/11) of manuscripts used sheep and only the 19% (2/11) used goats. The mean (± standard deviation) of experimental animals was 27.6 ± 12.3 per work. The 64% (7/11) of manuscripts involved a natural GIN infection, whereas the 36% (3/11) opted for an artificial infection, at its majority with the abomasal nematode *Haemonchus contortus*, and on one opportunity, a mixed infection with *H. contortus* and the intestinal nematode *Trichostrongylus colubriformis*.

Table 3 shows the plant species and chemical compounds involved in the analyzed works. Although we cannot identify a predominant botanical family, both Lamiaceae (n = 2) and Rutaceae (n = 2) accounted for the 36% of works (4/11). The use of a terpene-rich plant foliage was documented for two of the eleven works (18%). Consequently, the EsOi administration occupied the majority of works. Altogether, the analyzed works focused on EsOi, studied 76 PSM, among which were reported monoterpenes, sesquiterpenes, phenyl propanoids, hydrocarbons, acids, alcohols, aldehydes, phenols, acyclic esters, and lactones among others.

The outcomes dealing with the intake of terpenes and/or EsOi and GIN infection are presented in table 4. Broadly speaking, the AH activity of terpenes and EsOi was variable, with fecal egg excretion reduction values between 0 to 97.4%, according with the FECRT. The CnT approach was utilized in five of the eleven works (45%) and shows variable outcomes.

The *in vivo* approach on the evaluation of compounds with bioactive potential in small ruminants

The review presented here aimed to analyze some scientific manuscripts that evaluated the AH activity of terpenes and EsOi in small ruminants through the execution of *in vivo* trials. This approach, which directly involves the animal, has been an important component in the evaluation of synthetic and natural products within veterinary sciences. However, it is worthy to highlight that an official guideline for natural product evaluation in ruminants has not yet been published. For this reason, it is reasonable to emphasize in the current need for official documents endorsed by scientific committees. We, as part of the veterinary parasitologists community, are waiting for official organisms such as the World Association for the Advancement of Veterinary Parasitology (WAAVP) or the International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) publication of such guidelines in the near future.

Table 2. General information of manuscripts aimed to evaluate the anthelmintic activity of terpenes and essential oils through the *in vivo* approach in small ruminants.

Country	Test type	Species	Breed	n	Age	Experimental condition	Infection type	Reference
USA	FECRT CnT CnT	Goat	Boer, Alpine and Nubian	19 30 15	0-5 y 1-3.5 m 4-5 m	Pen	Natural MS, Hc MS, Hc	(62)
Brazil	FECRT CnT	Sheep	Hair	44 21	NS	Pen	Natural	(63)
Brazil	FECRT	Goat	NS	30	12-16 m	Field	Natural + MS, Hc	(64)
USA	FECRT	Sheep	Mixed	18	3 m	Pen	MS, Hc	(65)
Brasil	FECRT CnT	Sheep	Santa Inés	18	2 m	Pen	MS, Hc	(66)
USA	FECRT	Sheep	Blackbelly, Saint Croix	64	6 m	Pen	Natural	(67)
Brazil	FECRT	Sheep	NS	30	6-16 m	Pen	Natural	(68)
Brazil	FECRT	Sheep	Santa Inés	30	4-6 m	Pen	MS, Hc	(69)
Benín	CnT CnT	Sheep	Djallonke	15 15	4-6 m	Field Pen	Natural Mix, Hc + Tc	(70)
Brazil	FECRT	Sheep	Santa Inés	28	7 m	Pen	Natural	(71)
Brazil	FECRT CnT	Sheep	Santa Inés, Morada Nova	32 34	5 m 3 m	Pen	MS, Hc Natural	(72)

Country: USA United States of America; Test type: FECRT Fecal egg count reduction test, CnT controlled test; n number of experimental animals; Age: y years, m months; Infection Type: MS Monospecific, HC *Haemonchus contortus*, Tc *Trichostrongylus* colubriformis

Table 3. Plant species, administration mode, and chemical composition of tested material in the analyzed manuscripts.

Scientific name	Common Spanish name	Family	Presentation	Chemical compounds	Reference
Chenopodium ambrosioides	Epazote, paico	Amaranthaceae	Leaves, Essential oil	[4]: Ascaridole, p-cymene, α-terpinene, limonene	(62)
Lippia sidoides	Pimienta de romero	Verbenaceae	Essential oil	NS	(63)
Eucalyptus staigeriana	Eucalipto	Myrtaceae	Essential oil	[20]: α-pinene, β-pinene, β-myrcene, α-phellandrene, *O*-cymene, (+)- limonene, eucaliptol, γ-terpinene, α-terpinolene, β-linalool, β-citronellal, 4-terpineol, α-terpineol, *cis*-geraniol, Z-citral, *trans*-geraniol, E-citral, metil geranate, nerol acetate, and geraniol acetate	(64)
Citrus sinensis	Naranja valenciana	Rutaceae	Essential oil	*d*-limonene represented the 95% of solution[1]	(65)
Cymbopogon schoenantus	Zacate limón, limoncillo	Poaceae	Essential oil	[19]: Geraniol, geranial, neral, geraniol acetate, citronellol, (E) caryophyllene, linalool, citronellal, (E)-2-hexenal, γ-cadinene, caryophyillene oxid, N-decanal, 6-Metil-5-heptene-2-one, eugenol, citronelil acetate, α-humulene, cadine 1,4 diene, geranyl formate, α-murolene	(66)
Juniperus pinchotii	Enebro de mora roja	Cupressaceae	Leaves	The plant contained 'good' concentrations of condensed tannins and terpenoids	(67)
Thymus vulgaris	Tomillo	Lamiaceae	Essential oil	[13]: Thymol, p-cymene, γ-terpinene, linalool, β-duprezianene, α-pinene, camphor, sabinene *cis*-hidrate, isoborneol, trans-β-terpineol, myrcene, α-fenchene, (Z)-tagetone	(69)
Zanthoxylum zanthoxyloïdes	Fagara ‡	Rutaceae	Essential oil	[27]: γ-terpinene, undecane, valencene, decanal, 3-carene[2]	(70)
Mentha arvensis	Menta Japonesa	Lamiaceae	Essential oil	Menthol represented the 86.7% of essential oil[3]	(71)

‡ Common name in African countries; NS: Not Specificied; [1] A 40% emulsión with 40% Orange oil was administered; Chemical Compounds: The number between Brackets represent the number of secondary metabolites detected in the essential oil; [2] Reported 25 secondary metabolites, but those put in the table are the only reported; [3] Do not reported more secondary metabolites; (68) and (72) were excluded from this table because they used commercial solutions of monoterpenes

Table 4. Bioactive effect of plants and essential oils on gastrointestinal nematodes of small ruminants through the *in vivo* approach.

Test type	Material	Presentation	Dose	Results FECRT (↓ epg)	Results CnT	Reference
FECRT CnT CnT	*Chenopodium ambrosioides*	Leaves, Essential oil	0.2 mL/Kg 250 g leaves NR	NS	NS	(62)
FECRT CnT	*Lippia sidoides*	Essential oil	230-283 mg/kg	22.9 - 54.22%	Hc represented the 37.9% of infection whilst Tc represented the 62.1%	(63)
FECRT	*Eucalyptus staigeriana*	Essential oil	350 mg/kg	73.66%	‡	(64)
FECRT	*Citrus sinensis*	Essential oil	600 mg/kg[1]	94.9 – 97.4%	‡	(65)
FECRT CnT	*Cymbopogon schoenantus*	Essential oil	180-360 mg/kg	NS	NS	(66)
FECRT	*Juniperus pinchotii*	Leaves	30% inclusion	65%	‡	(67)
FECRT	Carvacryl acetate	Essential oil	250 mg/kg	65.9%	‡	(68)
FECRT	*Thymus vulgaris*	Essential oil	75-150-300 mg/kg	NS	‡	(69)
CnT CnT	*Zanthoxylum zanthoxyloides*	Essential oil	1-2 mL/Kg[2]	89%	The number of adult GIN was reduced. Female prolificity was also reduced	(70)
FECRT	*Mentha arvensis*	Essential oil	160-200 mg/kg	44.9 – 61.6% (NS)	‡	(71)
FECRT CnT	Encapsulated anethol and carvone	Essential oil	100-250 mg/kg*	55% at 47 days	Fertility of adult GIN was reduced	(72)

Test type: FECRT Fecal egg count reduction test, CnT Controlled test; Dose: mL milliliter, Kg kilogram, NS Not specified, mg milligrams; [1] Used peel orange essential oil; [2] Used essential oil from *Zanthoxylum zanthoxyloides* fruits; Results: ↓ epg reduction in excretion of gastrointestinal nematode eggs, NS not significative, ‡ does not apply; Hc *Haemonchus contortus*, Tc *Trichostrongylus colubriformis*, GIN Gastrointestinal nematodes

As a consequence, the works performed to date have utilized the official guidelines to assess the synthetic compounds effectivity (73) or some published data from field experts (74). These methodological strategies involve the study of plants / extracts AH properties over distinct stages of the GIN biological cycle (eggs, larvae, and adults) at the laboratory level, constituting the *in vitro* approach.

In vitro trials are cheaper and bring the possibility to examine a relatively higher number of samples in a shorter time period (75), thereby have been more used and documented. Based on our literature search, we can state that for every seven to ten manuscripts focusing on the *in vitro* approach, there is one manuscript dealing with the *in vivo* approach. However, *in vitro* trials do not face the multifactorial physiological conditions of animals in which: (i) there is a dynamic between quantities and concentrations of chemicals who enter into the system, (ii) the rate and sequence in which PSM are processed is dynamic and variable, (iii) high intakes of fresh material would be necessary to reach the concentrations that showed positive results on *in vitro* conditions, and (iv) rumen microbial populations have the capacity to develop adaptations toward PSM. Therefore, own to the difficulty to duplicate these factors, evaluate on the host represents the best choice to assess the AH value of plants and their derivatives (75).

Two methodologies assessing the AH activity of natural products are usually implemented on the *in vivo* approach (72):

Fecal egg count reduction test (FECRT); in which the bioactive material is administered to a group of animals and a quantitative follow-up of the number of GIN eggs per gram (EPG) in feces is estimated by establishing a time period (pre and pos). In this approach, the establishment of a control group is optional. Thus, researchers can define whether other experimental group do not receive the bioactive material or are free of GIN infection.

Controlled test (CnT); which is similar to FECRT, but the establishment of control groups is mandatory because experimental animals should be humanely euthanized to retrieve organs of the gastrointestinal tract where adult nematodes are located. After this step, counts and body measurements of adult GIN individuals are performed, which allows for comparison between experimental groups. Although this methodology is expensive and labor consuming, is the most reliable to evaluate the AH activity of natural products.

Experiences in the utilization of terpenes and essential oils over the small ruminants' gastrointestinal nematodes

The FECRT was implemented in all the analyzed manuscripts in the present review. The outcomes in EPG dynamics after administration of terpenes or EsOi were certainly ambiguous, showing activities considered as null (62,66,69), moderate (63,67,68), positive (64,70) and remarkable (63). Although these responses are not conclusive and were derived from a limited number of works, they allow us to detect a potential in the administration of terpene-rich resources with applicability on small ruminants. In the near future, it would be interesting to explore whether other factors could influence the bioactive properties of this natural products such as dose, bioavailability, plant harvest season, extraction method for terpene/EsOi obtention, and interaction between PSM. In the same way, factors such as administration route, productive performance, nutritional plane, physiological stage, and animal PSM adaptation level should be accounted for.

In the present review, five studies implemented the CnT approach to evaluate the AH activity of terpene-rich plants or EsOi and, similarly with the FECRT, the outcomes were variable. In the works of Ketzis et al (62) and Katiki et al (66), the administration of *Chenopodium ambrosioides* and *Cymbopogon schoenantus* EsOi, respectively had no effects on the adult GIN counts recovered after necropsy. Noteworthy outcomes were reported in Camurca et al (63), who observed certain selectivity of the *Lippia sidoides* EsOi over *Haemonchus contortus* populations. Also, the EsOi of *Zanthoxylum zanthoxyloides* fruits (70) and an encapsulated solution of the monoterpenes anethol and carvone (72) reduced the number of adult GIN, male size, and number of produced eggs in females.

The mechanisms used by terpenes and EsOi to negatively impair the GIN, are still unknown. However, it has been proposed that due to their hydrophobic nature, the cell membrane is the main target (76). These compounds enter GIN structures through transcuticular diffusion interfering the metabolism, avoiding vital functions on early developmental stages, and affecting some locomotion mechanisms (77). According with López and Pascual-Villalobos (78), EsOi show activity toward acetylcholinesterase receptors of vertebrates and invertebrates, producing a neurotoxic damage similar to organophosphates. Notwithstanding, is necessary to bear in mind that terpene / EsOi bioactivity might be as ample as their high number of identified molecules.

Research and development of natural AH products has been triggered because the growing populations of GIN resistant to commercial products. In this revision, ivermectin resistance on GIN populations was evident, by reporting EPG reductions of 67-85% (63), 35-54% (62), and 25% (67). In addition, some studies used the most recently introduced AH into the market (monepantel, Zolvix®) evidencing reduction levels of 100% (69), 96.4% (68) and, albeit the figures presented by Katiki et al (72) lacks a specific date, we can observe —clarifying that it requires a confirmation— some resistance level after 21 days of administration. These parasitological variables could be complemented with the assessment of physiological variables such as the packed cell volume (known as hematocrit), FAMACHA®, white cells count (66,67,70,72), and renal / hepatic function assessment (66,72). Additionally, the follow-up of productive variables such as the daily weight gain and feed conversion are of great importance given their applicability on different productive systems. In this sense, Whitney et al. (67) reported a reduction in the weight gain of Blackbelly and Saint Croix lambs after the inclusion of 30% *Juniperus pinchotii* in a balanced diet. These results were similar to those of Katiki et al (72) who reported a reduction in the daily weight gain on Santa Inés lambs. By contrast, Azando et al (70) reported that administration of EsOi from the fruit of *Z. zanthoxylum* did not affected neither the daily weight gain nor the final live weight of Djallonke lambs. Despite the fact that results suggest a negative trend over productive variables, future works should establish the *trade-off* costs between nutrition and health (79,80).

Terpene and EsOi possess a wide spectrum of biological activities that could be explored in veterinary sciences. A recent global review about terpenes in animals reported that 58% of 113 analyzed manuscripts were conducted on livestock species destined to human consumption (81). Currently, 80,000 plant species have been identified for their influence on animal health and productivity (82), therefore, it is necessary to understand the nature of their interactions with herbivores, and thus, suggest their nutritional and pharmaceutical properties in different small ruminant productive systems (83,84). These benefits could be characterized on functional foods or nutraceutical resources.

Interest conflict

The authors of the present study declare that any interest conflict exists with the publication of this manuscript.

REFERENCES

1. Mavrot F, Hertzberg H, Torgerson P. Effect of gastro-intestinal nematode infection on sheep performance: A systematic review and meta-analysis. Parasit Vectors. 2015; 8(1):1–11. http://dx.doi.org/10.1186/s13071-015-1164-z

2. Zajac AM, Garza J. Biology, Epidemiology, and Control of Gastrointestinal Nematodes of Small Ruminants. Vet Clin North Am - Food Anim Pract. 2020; 36(1):73–87. https://doi.org/10.1016/j.cvfa.2019.12.005

3. Kaplan RM, Vidyashankar AN. An inconvenient truth: global worming and anthelmintic resistance. Vet Parasitol. 2012; 186(1-2):70-78. https://doi.org/10.1016/j.vetpar.2011.11.048

4. Torres-Acosta JFJ, Mendoza-de-Gives P, Aguilar-Caballero AJ, Cuéllar-Ordaz JA. Anthelmintic resistance in sheep farms: update of the situation in the American continent. Vet Parasitol. 2012; 189(1):89-96. https://doi.org/10.1016/j.vetpar.2012.03.037

5. Scott I, Pomroy WE, Kenyon PR, Smith G, Adlington B, Moss A. Lack of efficacy of monepantel against *Teladorsagia circumcinta* and *Trichostrongylus colubriformis*. Vet Parasitol. 2013; 198(1-2):166-171. https://doi.org/10.1016/j.vetpar.2013.07.037

6. Van-de-Brom R, Moll L, Kappert C, Vellema P. Haemonchus contortus resistance to monepantel in sheep. Vet Parasitol; 2015; 209(3-4):278-280. https://doi.org/10.1016/j.vetpar.2017.09.010

7. Salles N, Love S. Resistance of *Haemonchus* sp. to monepantel and reduced efficacy of a derquantel / abamectin combination confirmed in sheep in NSW, Australia. Vet Parasitol. 2016; 228:193-196. https://doi.org/10.1016/j.vetpar.2016.08.016

8. Cerutti J, Cooper L, Torrents J, Suárez G, Anziani OS. Eficacia reducida de derquantel y abamectina en ovinos y caprinos con *Haemonchus* sp resistentes a lactonas macrocíclicas. Rev Vet. 2018; 29(1):22-25. http://dx.doi.org/10.30972/vet.2912782

9. Charlier J, Rinaldi L, Musella V, Ploeger HW, Chartier C, Rose Vineer H, et al. Initial assessment of the burden of parasitic helminth infections to the ruminant livestock industry in Europe. Prev Vet Med. 2020; 182:105103. https://doi.org/10.1016/j.prevetmed.2020.105103

10. Charlier J, van der Voort M, Kenyon F, Skuce P, Vercruysse J. Chasing helminths and their economic impact on farmed ruminants. Trends Parasitol. 2014; 30(7):361-367. https://doi.org/10.1016/j.pt.2014.04.009

11. Torres-Acosta JFJ, Hoste H, Sandoval-Castro CA, Torres-Fajardo RA, Ventura-Cordero J, González-Pech PG, et al. The art of war against gastrointestinal nematodes in sheep and goat herds of the tropics. Rev Acad (Pontif Univ Catól Paraná, Online). 2019; 17(1):39–46. https://periodicos.pucpr.br/index.php/cienciaanimal/issue/view/1977

12. Burke JM, Miller JE. Sustainable approaches to parasite control in ruminant livestock. Vet Clin North Am Food Anim Pract. 2020; 36(1):89-107. https://doi.org/10.1016/j.cvfa.2019.11.007

13. Torres-Acosta JFJ, Sandoval-Castro CA, Hoste H, Aguilar-Caballero AJ, Cámara-Sarmiento MA, Alonso-Díaz MA. Nutritional manipulation of sheep and goats for the control of gastrointestinal nematodes under hot humid and subhumid tropical conditions. Small Rum Res. 2012; 103(1):28-40. https://doi.org/10.1016/j.smallrumres.2011.10.016

14. Hoste H, Torres-Acosta JFJ, Quijada J, Chan-Pérez I, Dakheel MM, Kommuru DS, et al. Interactions between nutrition and infections with *Haemonchus contortus* and related gastrointestinal nematodes in small ruminants. Adv Parasitol. 2016; 93:239-351. https://doi.org/10.1016/bs.apar.2016.02.025

15. Heckendorn F, Bieber A, Werne A, Saratsis A, Maurer V, Stricker C. The genetic basis for the selection of dairy goats with enhanced resistance to gastrointestinal nematodes. Parasite. 2017; 24:32. https://doi.org10.1051/parasite/2017033

16. Bishop SC. A consideration of resistance and tolerance for ruminant nematode infections. Front Genet. 2012; 3:168. https://doi.org/10.3389/fgene.2012.00168

17. Claerebout E, Geldholf P. Helminth vaccines in ruminants: From development to application. Vet Clin North Am Food Anim Pract. 2020; 36(1):159-171. https://doi.org/10.1016/j.cvfa.2019.10.001

18. Ehsan M, Hu RS, Liang QL, Hou JL, Song X, Yan R, et al. Advances in the development of anti-*Haemonchus contortus* vaccines: Challenges, opportunities and perspectives. Vaccines. 2020; 8(3):555. https://doi.org/10.3390/vaccines8030555

19. Galindo-Barboza AJ, Torres-Acosta JFJ, Cámara-Sarmiento R, Sandoval-Castro CA, Aguilar-Caballero AJ, Ojeda-Robertos NF, et al. Persistence of the efficacy of copper oxide wire particles against *Haemonchus contortus* in sheep. Vet Parasitol. 2011; 176(2-3):201-207. https://doi.org/10.1016/j.vetpar.2010.11.012

20. Whitley NC, Dykes G, Vazquez J, Burke JM, Terrill T. Effect of Copper Oxide Wire Particles without anthelmintic treatment or anthelmintic treatment alone on gastrointestinal nematode (GIN) fecal egg counts in goats. J Anim Sci; 2021: 99(Suppl. S2). https://doi-org.ezproxy.javeriana.edu.co/10.1093/jas/skab096.079

21. Mahieu M, Arquet R, Fleury J, Bonneau M, Mandonnet N. Mixed grazing of adult goats and cattle: Lessons from long-term monitoring. Vet Parasitol. 2020; 280:109087. https://doi.org/10.1016/j.vetpar.2020.109087

22. Szewc M, De Waal T, Zintl A. Biological methods for the control of gastrointestinal nematodes. Vet J. 2021; 268:105602. https://doi.org/10.1016/j.tvjl.2020.105602

23. Comans-Pérez RJ, Sánchez JE, Al-Ani LKT, González-Cortázar M, Castañeda-Ramírez GS, Mendoza-de-Gives P, et al. Biological control of sheep nematode *Haemonchus contortus* using edible mushrooms. Biol Control. 2021; 152:104420. https://doi.org/10.1016/j.biocontrol.2020.104420

24. Borges DGL, Borges FA. Plants and their medicinal potential for controlling gastrointestinal nematodes in ruminants. Nematoda. 2016; 3e:92016. https://dx.doi.org/10.4322/nematoda.00916

25. García-Bustos JF, Sleebs BE, Gasser RB. An appraisal of natural products active against parasitic nematodes of animals. Parasit Vectors. 2019; 12(1):1-22. https://doi.org/10.1186/s13071-019-3537-1

26. Liu M, Panda SK, Luyten W. Plant-based natural products for the discovery and development of novel anthelmintics against nematodes. Biomolecules. 2020; 10(3):426. https://doi.org/10.3390/biom10030426

27. Mithöfer A, Boland W. Plant defense against herbivores: Chemical aspects. Annu Rev Plant Biol. 2012; 63:431-450. https://doi.org/10.1146/annurev-arplant-042110-103854

28. Agrawal AA, Weber MG. On the study of plant defence and herbivory using comparative approaches: how important are secondary plant compounds. Ecol Lett. 2015; 18(10):985-991. https://doi.org/10.1111/ele.12482

29. Ma T, Gao H, Zhang D, Shi Y, Zhang T, Shen X, Wu S, Xiang L, Chen S. Transcriptome analyses revealed the ultraviolet B irradiation and phytohormone gibberellins coordinately promoted the accumulation of artemisinin in *Artemisia annua* L. Chin Med. 2020; 15:67. https://doi.org/10.1186/s13020-020-00344-8

30. De Morais LAS. Influência dos fatores abióticos na composição química dos óleos essenciais. Hortic Bras. 2009; 27(2):S4050-4063. https://ainfo.cnptia.embrapa.br/digital/bitstream/item/143457/1/2009AA-051.pdf

31. Yang L, Wen KS, Ruan X, Zhao YX, Wei F, Wang Q. Response of plant secondary metabolites to environmental factors. Molecules. 2028; 23(4):762. https://doi.org/ 10.3390/molecules23040762

32. Neilson EH, Goodger JQD, Woodrow IE, Møller BL. Plant chemical defense: At what cost?. Trends Plant Sci. 2013; 18(5):250–258. http://dx.doi.org/10.1016/j.tplants.2013.01.001

33. Mueller-Harvey I, Bee G, Dohme-Meier F, Hoste H, Karonen M, Kölliker R, et al. Benefits of condensed tannins in forage legumes fed to ruminants: Importance of structure, concentration, and diet composition. Crop Sci. 2019; 59(3):861–885. https://doi.org/10.2135/cropsci2017.06.0369

34. Villalba JJ, Costes-Thiré M, Ginane C. Phytochemicals in animal health: Diet selection and trade-offs between costs and benefits. Proc Nutr Soc. 2017; 76(2):113–121. https://doi.org/10.1017/S0029665116000719

35. Muir J. The multi-faceted role of condensed tannins in the goat ecosystem. Small Rumin Res. 2011; 98(1-3):115–120. http://dx.doi.org/10.1016/j.smallrumres.2011.03.028

36. Hackmann TJ, Spain JN. Invited review: Ruminant ecology and evolution: Perspectives useful to ruminant livestock research and production. J Dairy Sci. 2010; 93(4):1320–1334. https://doi.org/10.3168/jds.2009-2071

37. Wang S, Alseekh S, Fernie AR, Luo J. The Structure and Function of Major Plant Metabolite Modifications. Mol Plant. 2019; 12(7):899–919. https://doi.org/10.1016/j.molp.2019.06.001

38. Pichersky E, Lewinsohn E. Convergent evolution in plant specialized metabolism. Annu Rev Plant Biol. 2011; 62:49–66. https://doi.org/10.1146/annurev-arplant-042110-103814

39. Staniek A, Bouwmeester H, Fraser PD, Kayser O, Martens S, Tissier A, et al. Natural products – modifying metabolite pathways in plants. Biotechnol J. 2013; 8(10):1159-71. https://doi.org/10.1002/biot.201300224

40. Dubois O, Allanic C, Charvet CL, Guégnard F, Février H, Théry-Koné I, et al. Lupin (*Lupinus spp*.) seeds exert anthelmintic activity associated with their alkaloid content. Sci Rep. 2019. 9(1):1-12. https://doi.org/10.1038/s41598-019-45654-6

41. Herath HMPD, Preston S, Jabbar A, García-Bustos J, Taki AC, Addison RS, et al. Identification of Fromiamycalin and Halaminol A from Australian marine sponge extracts with anthelmintic activity against Haemonchus contortus. Mar Drugs. 2019; 17:598. https://doi.org/10.3390/md17110598

42. Spiegler V, Liebau E, Hensel A. Medicinal plant extracts and plant-derived polyphenols with anthelmintic activity against intestinal nematodes. Nat Prod Rep. 2017; 34(6):627–643. https://doi.org/10.1039/c6np00126b

43. Oliveira Santos F, Ponce Morais Cerqueira A, Branco A, José Moreira Batatinha M, Borges Botura M. Anthelmintic activity of plants against gastrointestinal nematodes of goats: A review. Parasitology. 2019;146(10):1233–1246. https://doi.org/10.1017/S0031182019000672

44. Hoste H, Martínez-Ortíz-de-Montellano C, Manoralaki F, Brunet S, Ojeda-Robertos N, Fourquaux I, et al. Direct and indirect effect of bioactive tannin-rich tropical and temperate legumes against nematode infections. Vet Parasitol. 2012; 186(1-2):18–27. https://doi.org/10.1016/j.vetpar.2011.11.042

45. Piluzza G, Sulas L, Bullita S. Tannins in forage plants and their role in animal husbandry and environmental sustainability: A review. Grass Forage Sci. 2014; 69(1):32–48. https://doi.org/10.1111/gfs.12053

46. Zhou F, Pichersky E. More is better: the diversity of terpene metabolism in plants. Curr Opin Plant Biol. 2020; 55:1-10. https://doi.org/10.1016/j.pbi.2020.01.005

47. Bodas R, Prieto N, García-González R, Andrés S, Giráldez FJ, López S. Manipulation of rumen fermentation and methane production with plant secondary metabolites. Anim Feed Sci Technol. 2012; 176(1-4):78-93. https://doi.org/10.1016/j.anifeedsci.2012.07.010

48. Gershenzon J, Dudareva N. The function of terpene natural products in the natural world. Nat Chem Biol. 2007; 3:408-414. https://doi.org/10.1038/nchembio.2007.5

49. Mudianta IW, White AM, Suciati, Katavic PL, Krishnaraj RR, Winters AE, et al. Chemoecological studies on marine natural products: Terpene chemistry from marine mollusks. Pure Appl Chem. 2014; 86(6):995–1002. https://doi.org/10.1515/pac-2013-1111

50. Dudareva N, Negre F, Nagegowda DA, Orlova I. Plant volatiles: recent advances and future perspectives. Crit Rev Plant Sci. 2006; 25:417-440. https://doi.org/10.1080/07352680600899973

51. Bruce TJA, Pickett JA. Perception of plant volatile blends by herbivorous insects — Finding the right mix. Phytochemistry. 2011; 72(13):1605-1611. https://doi.org/10.1016/j.phytochem.2011.04.011

52. Benchaar C, Calsamiglia S, Chaves AV, Fraser GR, Colombatto D, McAllister TA, Beauchemin KA. A review of plant-derived essential oils in ruminant nutrition and production. Anim Feed Sci Technol. 2008; 145:209-228. https://doi.org/10.1016/j.anifeedsci.2007.04.014

53. García C, Montero G, Coronado MA, Valdez B, Stoytcheva M, Rosas N, et al. Valorization of Eucalyptus Leaves by Essential Oil Extraction as an Added Value Product in Mexico. Waste and Biomass Valorization. 2017;8(4):1187–1197. https://doi.org/10.1007/s12649-016-9695-x

54. Torres RNS, Moura DC, Ghedini CP, Ezequiel JMB, Almeida MTC. Meta-analysis of the effects of essential oils on ruminal fermentation and performance of sheep. Small Rumin Res. 2020; 189:106148. https://doi.org/10.1016/j.smallrumres.2020.106148

55. Cobellis G, Trabalza-Marinucci M, Yu Z. Critical evaluation of essential oils as rumen modifiers in ruminant nutrition: A review. Sci Total Environ. 2016; 545–546:556–568. http://dx.doi.org/10.1016/j.scitotenv.2015.12.103

56. Pavela R. Essential oils for the development of eco-friendly mosquito larvicides: A review. Ind Crops Prod. 2015; 76:174–187. http://dx.doi.org/10.1016/j.indcrop.2015.06.050

57. Bhavaniramya S, Vishnupriya S, Al-Aboody MS, Vijayakumar R, Baskaran D. Role of essential oils in food safety: Antimicrobial and antioxidant applications. Grain Oil Sci Technol. 2019; 2(2):49-55. https://doi.org/10.1016/j.gaost.2019.03.001

58. Srivastava A, Lall R, Sinha A, Gupta RC. Essential Oils. En Nutraceuticals in Veterinary Medicine. Gupta R, Srivastava A, Lall R (Eds.). Switzerland: Springer Nature; 2019. https://doi.org/10.1007/978-3-030-04624-8

59. Mukherje N, Mukherjee S, Saini P, Roy P, Babu S. Phenolics and terpenoids; the promising new search for anthelmintics: A critical review. Mini-Reviews Med Chem. 2016; 16(17):1415-1441. https://doi.org/10.2174/1389557516666151120121036

60. Abdel-Rahman FH, Alaniz NM, Saleh MA. Nematicidal activity of terpenoids. J Environ Sci Heal B. 2013; 48(1):16-22. https://doi.org/10.1080/03601234.2012.716686

61. André WPP, Ribeiro WLC, Oliveira LMB, Macedo ITF, Rondon FCM, Bevilaqua CML. Óleos essenciais e seus compostos bioativos no controle de nematoides gastrintestinais de pequenos ruminantes. Acta Sci Vet. 2018; 46:1522. https://doi.org/10.22456/1679-9216.81804

62. Ketzis JK, Taylor A, Bowman DD, Brown DL, Warnick LD, Erb HN. *Chenopodium ambrosioides* and its essential oils as treatments for *Haemonchus contortus* and mixed adult-nematode infections in goats. Small Rum Res. 2002; 44(3):193-200. https://doi.org/10.1016/S0921-4488(02)00047-0

63. Camurça-Vasconcelos ALF, Bevilaqua CML, Morais SM, Maciel MV, Costa CTC, Macedo ITF, et al. Anthelmintic activity of *Lippia sidoides* essential oil on sheep gastrointestinal nematodes. Vet Parasitol. 2008; 154(1-2):167-170. https://doi.org/10.1016/j.vetpar.2008.02.023

64. Macedo ITF, Bevilaqua CML, Oliveira LMB, Camurça-Vasconcelos ALF, Vieira LS, Oliveira FR, et al. Anthelmintic effect of *Eucalyptus staigeriana* essential oil against gastrointestinal nematodes. Vet Parasitol. 2010; 173(1-2):93-98. https://doi.org/10.1016/j.vetpar.2010.06.004

65. Squires JM, Foster JG, Lindsay DS, Caudell DL, Zajac AM. Efficacy of an orange oil emulsion as an anthelmintic against *Haemonchus contortus* in gerbils (*Meriones unguiculatus*) and in sheep. Vet Parasitol. 2010; 172(1-2):95-99. https://doi.org/10.1016/j.vetpar.2010.04.017

66. Katiki LM, Chagas ACS, Takahira RK, Juliani HR, Ferreira JFS, Amarante AFT. Evaluation of *Cymbopogon schoenanthus* essential oil in lambs experimentally infected with *Haemonchus contortus*. Vet Parasitol. 2012; 186(3-4):312-318. https://doi.org/10.1016/j.vetpar.2011.12.003

67. Whitney TR, Wildeus S, Zajac AM. The use of redberry juniper (*Juniperus pinchotii*) to reduce *Haemonchus contortus* fecal egg counts and increase ivermectin efficacy. Vet Parasitol. 2013; 197(1-2):82-188. https://doi.org/10.1016/j.vetpar.2013.06.010

68. Andre WPP, Ribeiro WLC, Cavalcante GS, Santos, JML, Macedo ITF, Paula HCB, et al. Comparative efficacy and toxic effects of carvacryl acetate and carvacrol on sheep gastrointestinal nematodes and mice. Vet Parasitol. 2016; 218:52-58. https://doi.org/10.1016/j.vetpar.2016.01.001

69. Ferreira LE, Benincasa BI, Fachin AL, França SC, Contini SSHT, Chagas ACS, Beleboni RO. *Thymus vulgaris* L. essential oil and its main component thymol: Anthelmintic effects against *Haemonchus contortus* from sheep. Vet Parasitol. 2016; 288:70-76. https://doi.org/10.1016/j.vetpar.2016.08.011

70. Azando EVB, Olounlade AP, Hounzangbe-Adote MS, Tam Ha TB, Fabre N, Valentin A. Contrôle des parasitoses gastro-intestinales ovines par l’huile essentielle de *Zanthoxylum zantoxyloïdes* (*Fagara zantoxyloïdes*). Rev Med Vet. 2017; 168:205-212. https://www.revmedvet.com/2017/RMV168_205_212.pdf

71. Chagas ACS, Figuereido A, Politi FAS, Moro IJ, Esteves SN, Bizzo HR, Gama PE, Chaves FCM. Efficacy of essential oils from planta cultivated in the Amazonian Biome against gastrointestinal nematodes in sheep. J Parasit Dis. 2018; 42:357-364. https://doi.org/10.1007/s12639-018-1007-x

72. Katiki LM, Araujo RC, Ziegelmeyer L, Gomes ACP, Gutmanis G, Rodrigues L, et al. Evaluation of encapsulated anethole and carvone in lambs artificially- and naturally – infected with *Haemonchus contortus*. Exp Parasitol. 2019; 197:36-42. https://doi.org/10.1016/j.exppara.2019.01.002

73. Wood IB, Amaral NK, Bairden K, Duncan JL, Kassai T, Malone JB, et al. World Association for the Advancement of Veterinary Parasitology (W.A.A.V.P.) second edition of guidelines for evaluating the efficacy of anthelmintics in ruminants (bovine, ovine, caprine). Vet Parasitol. 1995; 58:181–213. https://doi.org/10.1016/0304-4017(95)00806-2

74. Jackson F, Hoste H. In vitro methods for the primary screening of plant products for direct activity against ruminant gastrointestinal nematodes. En In Vitro Screening of Plant Resources for Extra Nutritional Attributes in Ruminants: Nuclear and Related Methodologies; Vercoe PE, Makkar HPS, Schlink AC (Eds.). FAO/IAEA Springer Edition: Dordrecht, The Netherlands; 2010.

75. Villalba JJ, Provenza FD. Challenges in Extrapolating In vitro Findings to In Vivo Evaluation of Plant Resources. En In Vitro Screening of Plant Resources for Extra Nutritional Attributes in Ruminants: Nuclear and Related Methodologies; Vercoe PE, Makkar HPS, Schlink AC (Eds.). FAO/IAEA Springer Edition: Dordrecht, The Netherlands; 2010.

76. Castilho CVV, Fantatto RR, Gaínza YA, Bizzo HR, Barbi NS, Leitão SG, et al. In vitro activity of the essential oil from *Hesperozygis myrtoides* on *Rhipicephalus (Boophilus) microplus* and *Haemonchus contortus*. Rev Bras Farmacogn. 2017; 27(1):70–76. http://dx.doi.org/10.1016/j.bjp.2016.08.005

77. Katiki LM, Barbieri AME, Araujo RC, Veríssimo CJ, Louvandini H, Ferreira JFS. Synergistic interaction of ten essential oils against *Haemonchus contortus* in vitro. Vet Parasitol. 2017; 243: 47–51. http://dx.doi.org/10.1016/j.vetpar.2017.06.008

78. López MD, Pascual-Villalobos MJ. Mode of inhibition of acetylcholinesterase by monoterpenoids and implications for pest control. Ind Crop Prod. 2010; 31:284–288. https://doi.org/10.1016/j.indcrop.2009.11.005

79. Costes-Thiré M, Laurent P, Ginane C, Villalba JJ. Diet selection and trade-offs between condensed tannins and nutrients in parasitized sheep. Vet Parasitol. 2019; 271:14–21. https://doi.org/10.1016/j.vetpar.2019.05.013

80. Landau SY, Provenza FD. Of browse, goats, and men: Contribution to the debate on animal traditions and cultures. Appl Anim Behav Sci. 2020; 232:105127. https://doi.org/10.1016/j.applanim.2020.105127

81. Da Silva JJM, Campanharo SC, Paschoal JAR. Ethnoveterinary for food-producing animals and related food safety issues: A comprehensive overview about terpenes. Compr Rev Sci Food Saf. 2021; 20(1):1-43 https://doi.org/10.1111/1541-4337.12673

82. Zeineldin MM, Sabek AA, Barakat RA, Elghandour MMMY, Salem AZ, Jiménez RM. Potential contribution of plants bioactive in ruminant productive performance and their impact on gastrointestinal parasites elimination. Agroforest Syst. 2020; 94(4):1415-1432. https://doi.org/10.1007/s10457-018-0295-6

83. Hoste H, Torres-Acosta JFJ, Sandoval-Castro CA, Mueller-Harvey I, Sotiraki S, Louvandini H, et al. Tannin containing legumes as a model for nutraceuticals against digestive parasites in livestock. Vet Parasitol. 2015; 312(1-2):5–17. http://dx.doi.org/10.1016/j.vetpar.2015.06.026

84. Torres-Fajardo RA, González-Pech PG, Sandoval-Castro CA, Torres-Acosta JFJ. Small ruminant production based on rangelands to optimize animal nutrition and health: Building an interdisciplinary approach to evaluate nutraceutical plants. Animals. 2020; 10(10):1-32. https://doi.org/10.3390/ani10101799