Agricultura Scientia 20: No 1: 61-73(2023)
https://doi.org/10.18690/agricsci.20.1.7

University of Maribor Press

Common Plant Bioactive Components Adopted in Combating Gastrointestinal Nematodes in Small Ruminant – A Review

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ABSTRACT

The high cost incurred by rural farmers on chemical anthelmintics, the reduction of the efficacy of this class of drugs and the development of resistant strains of Helminth has necessitate the search for suitable alternatives. However, there are still research gaps in the use plant secondary metabolites with no proper documentation of the active compound(s), standard administration route, mode of action and standardization of its use in small ruminant animals. This review focuses on the use of bioactive components of plants and plant extracts in combating gastrointestinal nematodes (GIN) in ruminant animals. It highlights the importance of the use of plants in both ruminant nutrition and health, the flaws of conventional methods of treatment and the need for suitable alternatives. It further documents the major bioactive components of plants used in the treatment of GIN in ruminants and their mode of action on nematodes' eggs, larva and adult worms. It is very clear that there exists a gap in research to validate the *in vitro* testing of some useful compounds *in vivo* owing to the identification of active components as most of them work in synergism with others, the dosing of the extracts is not uniform as the molecular weight of the selected compounds differs in most cases. Hence, this informs the need for collaborative research to validate the use of bioactive compounds and subsequent drug development to replace costly conventional anthelmintic that are constantly losing efficacy.

Key words: gastrointestinal nematodes, ruminants, bioactive compounds, anthelmintic

INTRODUCTION

The use of plants (shrubs, leguminous trees, browse plants, and other tree species) has been an old practice in ruminant animals' feeding/nutrition and health (Norton, 1994; Buxton and Redfearn, 1997; Chollet et al., 2013; Aruwayo and Adeleke, 2019). They are usually adopted to augment the shortage of feed during a certain period of the rearing season when the commonly used forages (especially grasses) are scarce or less nutritious (Leng and Fujita, 1997; Vandermeulen et al., 2018). The current climatic vagaries have further necessitated the search for suitable alternatives as the available grasses continue to depreciate in available nutrients during temperature extremes leading to poor productivity and poor health of livestock animals that depend solely on them. Also, the associated events associated with climate change favour the breeding/development of certain pathogens as well as their resistance (Nardone et al., 2010; Thornton et al., 2009; Rojas-Downing et al., 2017).

Most of these plants are adopted as they are evergreen, highly nutritious, contain plant secondary metabolites (PSM), enhance rumen digestion, and control gastrointestinal nematodes (GIN, Vandermeulen et al., 2018). Mostly, the crude protein (CP) content of these tree species, shrubs, herbs, and vines exceeds the recommended 7% CP for maintenance (NRC, 2007) requirements in ruminants, making them a suitable alternative with no loss in embedded nutrients. Although, some research (Milgate and Roberts, 1995; Waghorn and McNabb, 2003) document the negative effects of feeding these plants with PSMs since they are usually considered as anti-nutrients when used moderately, their adoption as feed resource is more beneficial. The PSM in

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plants has a specific mechanism employed by plants to resist damage by harmful insects and plant-eating animals, respond to environmental stresses, and mediating organismal interactions. Accumulation of PSM is a kind of plant survival mechanism in its ecosystem (Pang et al., 2021).

Plant secondary metabolites are generally grouped into phenolics, terpenoids and alkaloids where we have tannins, saponin and glycosides as part of them (Kabera et al., 2014). In turn, tannins, saponin and glycosides comprise many groups / classes that are useful bioactive component in small ruminant production. Plant bioactive components are chemicals in plants that are beneficial animals nutrition, health and well-being, they are available and are highly beneficial (Nirmala et al., 2014; Venthodika et al., 2021). In this study, we focused on few bioactive components (condensed tannins, hydrolysable tannins (phenols) and saponins (terpenoids)) commonly used to combat GIN in small ruminants.

The use of plants containing bioactive compounds for treatment of certain ailments in animals has been a long age practice that has its origin in traditional medicine and/or phytomedicine (Chopra et al., 1956; Said, 1969; Thirumalai, 2009; Rasool, 2012; Fayera et al., 2017). For decades, herbal plants have been employed in worm control, which is still in practice today. In ethnoveterinary practice, which emanated from herbal/traditional medicine, there is a range of plants or plant extracts used to combat gastrointestinal nematodes in most livestock species (IIRR, 1994). Medicinal plants are widely adopted to treat different types of disease or ailment varying from diarrhea, viral infection, bacterial infection, internal and external parasites, etc (Guarrera, 1999; Fayera et al., 2017). Their use (both *in vitro* and *in vivo*) as alternative anthelmintic has been well documented (Athanasiadou and Kyriazakis, 2004; Ademola et al., 2005; Bachaya et al., 2009; Ameen et al., 2012; Ahmed et al., 2020; Ifedibalu-Chukwu et al., 2020) but still with disparities with no valid conclusion on the mode of action and possible dosage for treatment.

In some cases, the use of certain plants with bioactive components gave positive results both *in vitro* and *in vivo*. In other cases, the positive inhibition reported in *in vitro* studies will yield no results *in vivo*. The discrepancies in these reported studies can be related to animal factors (breed, stage of growth, nutrition, sex etc.), plant factors (stage of growth harvested, regions and plant species specific), environmental factors (amount of rainfall and temperature extremes), plant parts, genetic profile, phenological stage, concentration and molecular weight of the bioactive component, and types of GIN being targeted (Cirak and Radusiene, 2019; Batista et al., 2021). In this study, therefore, we try to document various plants and plant parts with anthelmintic properties reported in scientific experiments (*in vitro* and *in vivo* studies) with their different class of bioactive components responsible for GIN control, their mode of action, and possible targeted species of GIN.

NEED FOR SUITABLE ALTERNATIVES

Significant economic losses in ruminant production resulting from gastrointestinal diseases caused by parasitic nematodes are serious problems that affect host productivity (Moreno et al., 2010, Felice, 2015). The caution/ban in the use of synthetic anthelmintic treatment due to the developed resistance by some gastrointestinal nematode populations, most especially Haemonchus (Epe and Kaminsky, 2013) and the residual effect down the food chain has resulted in a search for a more effective alternative.

The control of gastrointestinal nematodes using secondary metabolites from plants used in indigenous herbal medicine has been well adopted to eliminate the residual effect in animals and down the food chain and there has been no reported study that detailed the resistivity of nematodes to plant bioactive components (Athanasiadou et al., 2007). Several researchers have reported the use of medicinal plants to be safe, sustainable, and environmentally acceptable (Akhtar et al., 2000; Athanasiadou et al., 2007; Shen et al., 2010; Durmic and Blache, 2012; Hernández et al., 2014).

Although, it has also been reported that certain plants or their extracts cause inflammation of the host gastric and intestinal mucosal (Borba et al., 2010). Therefore, the selection of a plant-based on its anthelmintics properties should be more beneficial than its anti-nutritive properties (Athanasiadou et al., 2007). The list of plants and plant parts used in controlled experiments (*in vitro* and *in vivo*).

Tannins

Tannin-rich plants usage in the control of GIN can be termed an orthodox and/or natural alternative to common chemical anthelmintics. According to Hoste et al. (2012, 2016), tannin-rich plants are the most studied group of bioactive resources in ethnoveterinary, animal health and veterinary medicine. Tannins are grouped into two subgroups, hydrolyzable tannins (HT) and condensed tannins (CT) (proanthocyanidins) with molecular structures that are distinctively different (Min and Hart, 2003). Naumann (2017) described hydrolyzable tannins as polyol core molecules which are mainly glucose units whose hydroxyl group from core polyols can be esterified with gallic acid. Condensed tannins on the other hand are the proanthocyanidins which consist of oligomers and/or polymers of flavan-3-ol subunits.

Condensed tannin as a bioactive anthelmintic

Based on the aforementioned need for alternatives to chemical anthelmintics, several research has been done to investigate the effect of tannin (without being classified), HT and CT on gastrointestinal nematodes. For clarity, research was taken further to specify the type of tannin present and the effect on the said gastrointestinal nematode(s). CT interferes with the feeding of *Haemonchus contortus*, *Trichostrongylus colubriformis* and *Trichostrongylus circumcinta larvae* using CT extracts of *Acacia molissima* (Minho et al., 2008). In another study by the same author, a reduction in faecal egg count (FEC) and gravid adult *Haemonchus contortus* was documented in sheep administered A. *molissima* extracts (150 gkg^{-1} CT dry matter, DM) extracts (Minho et al., 2008b). CT from Quebracho extract reduced *H. contortus, T. colubriformis* and *Nematodirus battus* FEC of sheep when fed at the rate of 16% weight per weight Quebracho in feed while the GIN was reduced with 8% w/w Quebracho in feed (Athanasiadou et al., 2001). CT rich *Sericea lespedeza* decreased the FEC of Boer goat by 84.6 and 91.9% (Terril et al., 2009).. In naturally infected sheep offered *Acacia negra* (18% CT), a significantly lower FEC was observed at week 8 for different species (*Trichostrongylus colubriformis, Haemonchus contortus, Oesophagostomum columbianum, Cooperia sp., Strongyloides papillosus, Trichuris globulosa and Moniezia expansa*) of gastrointestinal nematodes (Cenci et al., 2007). Dubey et al. (2012) fed CT from 3 different plants (*Ficus infectoria, Psidium guajava* and *Ficus bengalensis*) at varying levels (0, 1 and 2%) to goat kids, it was documented that 2.0% level of CT decreased the FEC. A 42.2, 63.1 and 65.4% decrease in larval migration of *H. contortus* was observed in CT extracted from *Acacia angustissima var. hirta, Lespedeza stuevei* and *Leucaena retusa*, respectively. while CT from *Desmanthus illinoensis, Lespedeza cuneata*, and *Acaciella angustissima* had less effect against third-stage larvae (Naumann et al., 2014a). GIN burden (*Teladorsagia spp* and *Nematodirus spp*) of lambs was reduced through feeding of CT-rich sainfoin [*Onobrychis viciifolia*] (Werne et al., 2013). In an experiment conducted by Gaudin et al. (2016), feeding sainfoin pellet reduce the overall FEC by 50% in sainfoin supplemented group compared to the control group. Iqbal et al. (2007) observed a direct effect of CT through inhibition of egg hatching *in vitro* as well as a reduction in FEC in CT supplemented group. Extracted CT from 7 different herbages inhibits the larva migration of Trichostrongylus colubriformis.

HYDROLYZABLE TANNINS AS BIOACTIVE ANTHELMINTIC

HT represents a class of bioactive compounds produced by plants with some specific antioxidant, anti-cancer, anti-ulcerative, anti-inflammatory and anti-parasitic properties (Okuda and Ito, 2011). Unlike CT, HT are not usually tested for its anthelmintic efficacy as do for CT either *in vitro* or *in vivo* for its anthelmintic efficacy, which may be attributed to the reported toxicity for some documented feeding experiments, however, the available data on experiment tested via *in vitro* showed higher lethality and malformation of both eggs and larva of the targeted GIN species (del Carmen Acevedo-Ramírez et al., 2020). The extracted tannins used in most of the studies are commercially sourced and standardized. This can contribute to most successes reported in most of the reviewed studies (Hervas et al., 2003; Fructos et al 2004) as they are pure tannin produced under standardized procedures. Katiki et al., (2013) examined plants for both condensed and hydrolyzable tannins anthelmintic activities on *Caenorhabditis elegans*. Higher concentrations of HT (20 and 25 mg ml^{-1}) extracts were lethal to *C. elegans* compared to those from CT. The tested plants were also noted for their antioxidant capacity. In a study by Wolinsky et al. (1996), neem (*Azadirachta indica*) HT (85%) reflect no anthelmintic activities, the higher concentration of HT is rather linked to its antibacterial effect. However, Iqbal et al (2010) reported a decrease in FEC in artificially infected sheep when administered methanolic extract of *A. indica*. Similarly, feeding fresh neem leaves to sheep resulted in a reduction in *Haemonchus, Oesophagostomum* and *Trichostrongylus* load (Chandrawathani et al., 2006). Mukka et al. (2008) also documented a reduced anthelmintic activity of HT in an *in vitro* study using a tea plant (*Camellia sinensis* L.) against *C. elegans*. In an experiment targeting the adult stage of *H. contortus*, HT from chestnut (*Camellia sinensis*) reduced motility with subsequent death of the adult GIN. The higher the dosages the higher the lethality effect (del Carmen et al., 2019). Engstrom et al (2016) also documented that the most active compounds against egg hatching of *H. contortus* had a molecular weight of between 940 Da which can vary with the structure of the compounds. The concentration of HT from chestnut extract at 2 mg/ml revealed the destruction of L3 stage of *H. contortus* under electron microscope (del Carmen Acevedo-Ramírez et al., 2020).

Saponins as bioactive anthelmintic

Saponins are heterogeneous chemical group with a variety of biological effects (health management and immune stability) in ruminant livestock. It is somehow avoided in some feeding experiments as it has been documented to have a bitter taste which limits the voluntary intake in ruminant animals (Heng et al., 2006). They have however been tested in the control of gastrointestinal nematodes in livestock animals, but the research available is limited when compared with that of CT. In an experiment by Wahyuni et al. (2019), they related the larval migration inhibition of *H. contortus* documented to the presence of bioactive compounds like tannin, flavonoids, alkaloids, saponin, phenol hydroquinone and triterpenoids isolated from different *Cassia* species used. In a similar study with sheep (strongyle eggs), at high concentration (88.3% of the total aglycones and echinocystic acid (90.1%)) various tested *Medicago* spp extracts had similar anthelmintic properties compared to Thiabendazole (3 μg/ml) (Maestrini et al., 2020).

A 38% decrease in FEC was reported when sheep were fed with 1.5% saponin of *Quillaja saponaria* bark origin (Ademola and Ellof, 2010). Higher egg hatch and larva development inhibition observed by Copani et al., (2013) was related to saponin contents from extracts of *Combretum molle*. In an *in vitro* trial by Santos et al. (2018) with different saponin compounds against goat parasitic nematodes, aescin showed 99%/EC50 (half maximal effective concentration) at 0.67 mg/ml while digitonin gave 45%. Larval motility was reduced by digitonin and hecogenin acetate at varying concentrations. Correlation between the anthelmintic activities of various plants used in traditional folklore and the bioactive compounds revealed a positive relationship between the anthelmintic activities and active saponins present in the selected plant species (Njonge et al., 2013). In a selective grazing experiment by Kotze et al. (2011), the observed anthelmintic potential of *Rhagodia preisii* cannot be linked to the presence of tannin, saponin and oxalates in the plant but the presence of other shrubs in the paddock. In an *in vivo* experiment with growing lambs, administration of *Salix babylonica* and *Leucaena leucocephala* extracts led to a reduction in both egg and worm count of different GIN species and both plants were documented to contain total phenolics and saponins (Hernandez et al., 2014). Gomes et al. (2016) reported lower (10.8-79%) anthelmintic efficacy for egg hatch inhibition of saponin fraction (SF) from *Zizyphus joazeiro* while SF was effective for cytotoxic evaluation, hence preventing the hatching of the nematodes egg. Botura et al. (2013) reported that saponin and flavonoid fractions extracted from *Agave sisalana* showed high *in vitro* anthelmintic activity against GIN in goats.

Flavonoids as bioactive anthelmintic

In animal studies (*in vivo*), flavonoids were rarely isolated for its anthelmintic function but rather reported with its presence among other tannins. However, two flavonoids (luteolin-7-β-O-glucopyranoside and quercetin-3-O-β-glucopyranoside) isolated from *Vicia pannonica* were found to have 100% lethality on larva migration of sheep trichostrongylosis through destruction of the larva (Kozan et al., 2013). A study by Azando et al. (2011) concluded that the anthelmintic activity of *Newbouldia laevis* and *Zanthoxylum zanthoxyloïdes* extracts was majorly due to flavonoids and tannins since the control experiment were marred with polyethelene glycol (PEG) and *Polyvinyl polypyrrolidone* (PVPP). The use of PEG and PVPP has always been adopted to test the effectiveness of tannins as anthelmintics as it binds to the tannins thereby lowering concentrations / bioavailability (Mahlo and Chauke, 2012). In a mathematical model, a synergistic effect of CT and two different flavonoids (quercetin and luteolin) was said to show anthelmintic activities in larva exsheathment of *H. contortus* (Klongsiriwet et al., 2015).

MODE OF ACTION OF DIFFERENT BIOACTIVE COMPONENTS

The mode of action of the tanniferous compounds varies, here we try to document the assumptions of different authors. Jain et al. (2013) stated that tannins can render inaccessible the free protein in the digestive tract, hence, preventing the availability of nutrients for larva use, thereby resulting in larva starvation. Ingestion of CT by insect or larva can cause autolysis when the CT bind with the intestinal mucosa (Schultz, 1989). Tannins can also act directly by reducing the metabolism rates in the intestines thus inhibiting oxidative phosphorylation, also resulting in larval death (Kateregga et al., 2014). Similarly, energy production in the GIN cells can be inhibited by tannins and flavonoids by preventing vital biochemical reactions. The binding of CT to larvae cuticle that is rich in glycoprotein (Thompson and Geary, 1995) can lead to larvae death (Sharma and Prasad, 2014).

Condensed tannins

Muller-Harvey and McAllan (1992) opined that the chemical nature of tannin also affects the variation in responses from different worm species. Survival of these nematodes is related to abomasa pH, in this case, the tannin-protein complex formed may dissociate with an increase or decrease in pH (Cenci et al., 2007). Hoste et al. (2012) noted that extracted CT alters the cuticle (outer covering) of nematode when treated with extracted condensed tannin thereby disrupting both digestive and reproductive processes. According to Klongsiriwet et al. (2015), CT works better in synergy with other bioactive compounds. Anthelmintic activity of CT can be based on the weight of the polymers, Naumann et al. (2014a) and Barrau et al. (2005) thought that the anthelmintic potential of smaller CT polymers (< 500 Da) is higher than that of CT with larger polymers (< 2000 Da). Contrarily, this assertion was opposed by Quijada et al. (2015) and Desrues et al. (2016), who linked the variation to either the differences in extraction and purification of the CT and to the types of targeted gastrointestinal nematodes. CT also affect the fecundity of the female nematodes.

Hydrolyzable tannins

The proposed mechanism for the activity of hydrolyzable tannins is through binding to collagen proteins and proteins rich in proline and hydroxyproline on the cuticle of the larvae (Engstrom et al., 2016). The ability of HT to bound to the surface of the eggshell, presumably via tannin–protein interactions, and either disturbed the proteins that cause the actual hatching process as suggested in previous studies (Molan and Faraj, 2010) or the HT coat around the egg simply mechanistically disabled the penetration of the larvae through the eggshell (Engstrom et al., 2016). The HT coat could also disable vital functions such as oxygen exchange between the inside and outside of the egg. This is similar to the condensed tannins mechanism (Athanasiadou et al., 2001). The potency of various groups of tannins at the doses of 20 and 25 mg/mL, HT-rich, or both CT-and HT-rich, extracts were reportedly more lethal to adult C. elegans than extracts containing only CT (Katiki et al., 2013). This is also related to the type of HT or CT present, while the presence of high concentration HT in a particular plant does not relate to its anthelmintic activity. One of the simplest parameters to be measured from HT structures is their molecular weight (Moilanen et al., 2013). Engstrom et al., (2016) showed that compounds with a molecular weight below 700 Da or above 2000 Da had no or very little significance on the egg hatching of *H. contortus*. However, the ability to achieve a relatively good activity at a low concentration or a very high activity at a high concentration depends on the concentration of the given tannin in a plant product. HT is also noted to disrupt the cuticle around the mouth and reproductive organs of GIN. It was noted that the cuticle destruction increased with time till the loss of the cuticle structure (de Carmen et al., 2019). The potency reported by de Carmen et al. (2019) can be linked to the use of standardized HT which has eliminated the effect of different plant and environmental variables. Engstrom et al. (2016) linked the relationship between the HT and its anthelmintic activities to the type and functional groups as well as the monometric linkage of the HT. Hydrolyzable tannin's biological activity is reportedly more potent than condensed tannins. This could mean that the preferred level of administration for the use of condensed tannin could be toxic at the same level for HT. However, research confirmed that lower doses of HT might not lead to any form of toxicity in animals. HT's ability to improve the nutrients absorption and the productive performance of animals has been reported without any adverse effects (Frutos et al., 2004) and the *in vivo* anti-parasitic effect has also been suggested (Corona-Palazuelos et al., 2016).

Saponins

Saponins are natural compounds with great anthelmintic potentials (Gomes et al., 2016; Santos et al., 2018). They reportedly affect some cell membrane (Doligalska et al., 2011) components causing the formation of micelle-like aggregates which disturbs the function of the cell membrane thereby resulting in cell lysis (Doligaliska et al., 2011). Saponins usually form complexes with components of the membranous cell at different stages of the nematode life cycle, hence, enhancing increased permeability of the cell membrane and subsequent death of the GIN (Tava and Avato, 2006; Vo et al., 2017). Saponins restrict feed intake, limit nutrients available for the helminths, then starvation as well as death (Kateregga et al., 2014). Plants such as *Medica* spp for the saponin content (Maestrini et al., 2019), *Cinnamomum verum* bark extract (Williams et al., 2015), *Aloe ferox* and *Senecio congestos* have been analyzed *in vitro* and are found to be rich in biologically active secondary metabolites (Teedzai et al., 2013). Maestrini et al. (2019) reported that the mode of action of saponins on GIN eggs is unspecified but related it to the earlier assertion of membrane permeability which makes it easier to penetrate the eggs with subsequent disruption of the egg content as well as inhibiting the development of the nematode larva. It is also hypothesized that saponin may aid reduction in GIN eggs by disrupting the enzymatic process during egg hatching (Gomes et al., 2016). The chemical structure/component/ molecular weight of the bioactive components is also believed to play a key role in the bioactivity of saponins. Santos et al. (2018) observed a cytotoxic activity of saponin on vero cells reflected from alteration in the morphology of the cell. This was confirmed by Paris et al. (2011) and Platonova (2015) who noted that the alteration in the cell shape as a result of the increase in cell permeability can be linked to cell death. Hernandez et al. (2014) believed that the reduced FEC and GIN burden could be attributed to the increase in administration intensity which can as well affect the fecundity of the female worms.

CONCLUSIONS

The mode of action of CT, HT, saponin and other bioactive compounds is similar in relation to the effect on eggs, larva (L1-L3) and adult worms. But their effects as stated in literature with the scope of reported experimental research, however, it is necessary for uniformity research that will specify the actual dosage required for *in vitro* egg hatching and larval migration inhibition. It is also crucial to perform guided biological classification of various plant extracts and fractions to identify the active compound. This will also call for multidisciplinary research to involve biochemists, pharmacists, parasitology, veterinary specialist and animal scientist to test various results from *in vitro* experiments for actual validation and adoption for use in animal experimentation. Thus, this can be used to develop an herbal-based anthelmintic with effective dosage. Conclusively, the anthelmintic efficacy of these bioactive compounds against different gastrointestinal nematodes can be linked to combined effects from egg cell wall damage, larva deformation and feeding disruption, inhibition of nematode motility and impairment of reproductive activity.

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APPENDIX

Table 1: List of plants and plant parts used in controlled experiments (in *vitro* and in *vivo*)

Plant/tree species used	Part used	Targetted class of worm	Bioactive ingredient	References
Achillea whilhelmsii (yarrows) *Teucrium stocksi* (germanders)	Aerial part	Adult roundworm, Tapeworms	Saponin	Ali et al., 2011
Crinum macowanii (cape coast lily) *Gunnera perpensa* (river pumpkin) *Nicotiana tabacum* (tobacco) *Sarcostemma viminale* (rapunzel plant) *Vernonia amygdalina* (bitter leaf) *Zingiber officinales* (ginger) Zizyphus mucronata (buffalo thorn)	Aerial part/ leaves	L3 nematode larvae	Alkaloids and tannin	Fomum and Nsahlai, 2017
Robes nigrum (black currant) *Tilia* L. (tilia) *Salize* spp (willow) *Trifolium repens* (White clover)	Leaves Flowers Bark Flower	*Oesophagostomum dentatum*	Condensed tannin	Williams et al., 2014
Vernonia lasiopus (iron weed) *Erythrina abyssinica* (coral tree) *Aspilia pluriseta* (dwarf aspilia) *Entada leptostachya* (Entada)	Leaves Bark Leaves Roots	*Heamonchus* *Mecistocirrus* *Ostertagia Cooperia* *Bunostomum* *Trichostrogylus* *Strongyles*	Saponin	Njonge et al., 2013
Chestnut tree (*Camellia sinensis*)	Tree extract	*Heamonchus contortus* (adult stage)	Hydrolysable tannin	Acevedo-Ramirez et al., 2020
Rhagodia preissii	Leaves	*T. colubriformis* *Haemonchus contortus* (larvae)	Saponin and tannin	Kotze et al., 2011
Medicago sativa (lucerne) *Medicago polymorpha* (burr medic)	Leaves	*Trichostrongylus* spp *Oesophagostomum* spp *Cooperia* spp *Haemonchus* spp *Chabertia*	Saponin	Maestrini et al., 2020
Momordica charantia (Bitter gourd)	Fruits and leaves	*Ascaris* suum *Ascaridia* galli *Fasciola hepatica* *Stellant chasmus falcatus* *Strongyloides* spp	Saponins Flavonoids Anthocyannins	Poolperm and Jiraungkoorskul, 2017.
Balanites aegyptiaca (dersert date) *Tamarindus indica* (tamarind) *Celtis toka* (Celtis toka)	Foliage	*Heamonchus contortus*	Condensed tannin	Assefa et al., 2017
Epilobium angustifolium (Willow herb) *Potentilla anserine* (Silverweed) *Geum urbanum* (herb bennet) *Quercus robur* (English oak) *Lythrum saliciana* (purple loosetrife) *Filipedual ulmaria* (meadowsweet) *Geranium sylvaticum* (wood cranesbill) *Rosa rugose* (rose) *Rosa pimpinellifolia* (burnet rose)	Leaves and flowers	*Haemonchus contortus*	Hydrolyzable tannin	Engstrom et al., 2016.
Artemisia herba-alba (white wormwood) *Punica granatum*	Fresh flower (stem and leaves) Peel and roots	Adult and egg of *Haemonchus contortus*	Alkaloids Saponins Flavonoids Tannins Glycosides Phenols	Ahmed et al., 2020

Table 1: List of plants and plant parts used in controlled experiments (in *vitro* and in *vivo*) (*cont.*)

Plant/tree species used	Part used	Targetted class of worm	Bioactive ingredient	References
Parkia biglobosa (African locust bean)	Seeds and leaves	Nematodes eggs	Alkaloids Saponins Cardenolides Alkaloids Cardenoloides Saponin tannin	Soetan et al., 2018
Ziziphus nummulana (wild jujube) *Acacia nilotica* (gum Arabic tree)	Bark fruit	Adult female and eggs of *Haemonchus contortus*	Alkaloids Flavonoids Saponins Flavonoids Triterpenoids Flavonoids Tannins Cyanogenic glucosides	Bachaya et al., 2009
Carica Papaya (pawpaw)	Seeds	*Heterakis gallinarium* *Trichostrongylus tenium* *Ascaridia galli*	Papain	Ameen et al., 2012
Spondias mombin (hog plum)	Leaves	*Haemonchus* spp *Trichostrongylus* spp *Oesophagostomum* spp *Strongyloides* spp Trichuris spp	Tannin and saponins	Ademola et al., 2015
Acacia nilotica (gum Arabic tree)	Bark and leaves	*Haemonchus* contortus	Flavonoids and tannins	Badar et al., 2011
Acacia nilotica (gum Arabic tree) *Acacia karoo* (sweet thorn)	Leaves	*Haemonchus* contortus	Tannin	Kahiya et al., 2003
Acacia salicina (willow wattle) *Acacia nilotica* (gum Arabic tree) *Eucalyptus corymbia* (bloodwood) *Casuarina cunninghamiana* (river she-oak) *Eucalyptus drepanophylla* (Queensland Grey Ironbark)	Leaves	*Haemonchus contortus* *Trichosrongylus colubriformis*	Tannin and polyphenol	Moreno et al., 2012

Običajne rastlinske bioaktivne sestavine, uporabljene za zatiranje gastrointestinalnih ogorčic pri drobnici – pregled

IZVLEČEK

Visoki stroški, ki jih imajo kmetje zaradi kemičnih antihelmintikov, zmanjšanje učinkovitosti te skupine zdravil in razvoj odpornih sevov ogorčic zahtevajo iskanje ustreznih alternativ. V raziskavah še vedno obstajajo številne vrzeli pri uporabi rastlinskih sekundarnih metabolitov glede (ne)ustreznosti dokumentacije o aktivnih spojinah, načina delovanja in standardizacije njihove uporabe pri drobnici. Ta pregledni članek se osredotoča na uporabo bioaktivnih sestavin rastlin in rastlinskih izvlečkov za zatiranje gastrointestinalnih ogorčic (GIN) pri prežvekovalcih in poudarja pomen uporabe rastlin v prehrani in zdravju prežvekovalcev, pomanjkljivosti konvencionalnih metod zdravljenja in potrebo po ustreznih alternativah. Nadalje dokumentira glavne bioaktivne sestavine rastlin, ki se uporabljajo pri zdravljenju GIN pri prežvekovalcih in njihov način delovanja na jajčeca, ličinke in odrasle osebke ogorčic. Zelo jasno je, da obstaja vrzel v raziskavah za potrditev *in vitro* testiranja nekaterih uporabnih spojin *in vivo* zaradi identifikacije aktivnih sestavin, saj večina od njih deluje v sinergizmu z drugimi, odmerjanje izvlečkov pa ni enotno, saj se molekulska masa izbranih spojin v večini primerov razlikuje. Iz rega razloga je potrebno izvesti skupne raziskave, na osnovi katerih bi lahko potrdili uporabnost bioaktivnih spojin in nato razvili zdravila, ki bi nadomestila drage konvencionalne antihelmintike, ki nenehno izgubljajo učinkovitost.

Ključne besede: gastrointestinalne ogorčice, prežvekovalci, bioaktivne spojine, antihelmintik