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Using plant bioactive materials to control gastrointestinal tract helminths in livestock☆

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ABSTRACT

Use of plants containing bioactive compounds to control of helminths in the gastrointestinal tract, either as phytotherapeutic or nutraceutical options, has been a growing research area in recent years. We discuss strategies to identify viable candidate compounds with *in vitro* and *in vivo* anthelmintic properties. We also discuss factors which may influence *in vitro* and *in vivo* results, and difficulties of translating *in vitro* results to *in vivo* conditions are considered using experiences with small ruminants, as most published research on phytotherapeutic or nutraceutical materials has been in sheep and goats and has been reviewed recently. Therefore, we summarize results of various plant bioactive materials against helminth parasites in the gastrointestinal tract of cattle, deer, rabbits, pigs and poultry, and conclude that many plant materials have resulted in promising results in many farm animal species besides sheep and goats. These bioactive materials may be used as a part of sustainable helminth control strategies.

1. Introduction

The possibility of using plant bioactive compounds to control helminth parasites in the gastrointestinal tract, either as phytotherapeutic or nutraceutical options, has been a growing research area. There have been several review papers dealing with positive and negative effects of these compounds on animal physiology, performance and health (Hoste et al., 2005; Mueller-Harvey, 2006; Rochfort et al., 2008). Also, the anthelmintic (AH) effect of one class of bioactive compound (*i.e.*, tannins), contained in many plants, against gastrointestinal nematodes (GIN) of small ruminants (*i.e.*, sheep and goats) was recently reviewed (Hoste et al., 2012), including all available information of direct and indirect effects of AH against GIN. Hoste et al. (2008) provided a definition for phytotherapeutic and nutraceutical activity, as well as descriptions of several methodologies in an attempt to suggest guidelines for investigating possible AH effects of bioactive plants against GIN.

Abbreviations: AH, anthelmintic; AMIA, adult motility inhibition assay; CT, condensed tannins; EHA, egg hatch assay; GIN, gastrointestinal nematodes; LDA, larval development assay; LEIA, larval exsheathment inhibition assay; LFIA, larval feeding inhibition assay; LMIA, larval migration inhibition assay; PEG, polyethylene glycol; PSM, plant secondary metabolites; PVPP, polyvinylpolypyrrolidone; SL, sesquiterpene lactones.

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Other papers have discussed practical methods to use tannin containing materials against GIN of small ruminants, while considering practicalities in commercial production systems (Alonso-Díaz et al., 2010a; Torres-Acosta et al., 2012). However, less effort has been given to gathering information in relation to livestock species other than sheep and goats. Furthermore, very limited information is available on other types of plant bioactive compounds, or on the effects of those compounds against other types of helminths.

This review discusses some aspects which need to be considered when investigating *in vitro* and *in vivo* AH effects of phytotherapeutic or nutraceutical materials, and also presents a brief description of available results against helminths of cattle, deer, rabbits, pigs and poultry.

2. Choosing the right candidates to evaluate for anthelmintic activity

Many researchers have used ethnoveterinary information to choose possible plant candidates which could be tested as AH against internal parasites of humans and animals (Waller et al., 2001; Githiori et al., 2005, 2006). Another important source of information is direct use of questionnaires and interviews with key groups such as traditional healers (Sudarsanam et al., 1995; Ali, 1999; Matin et al., 2001) or farmers with practical experience (Smidt and Brimer, 2005). Many projects use these sources of information when trying to obtain valid information on plants which people recommend in the case of problems of the gastrointestinal tract, both in humans and farm animals. However, some may start by looking for anti-parasitic effect of plants which are helpful for the stomach or to control diarrhea. These clinical signs could be related to different gastrointestinal ailments and not necessarily parasitic helminths. That parasites are hidden in the gastrointestinal tract complicates information gathering on which materials may affect those parasites. It is also important to consider that a medicinal remedy which may work in humans may not be useful in other animal species, such as ruminants.

Some research groups choose to follow the promising path of studying plants with bioactive components, either as phytotherapeutics or nutraceuticals, which have been shown to have a high level of anti-parasitic activity against the parasite of interest. This option could be followed for those parasites with similar life cycles in other hosts. A good example is the study of plants containing large amounts of cysteine proteinases, which are proteolytic enzymes in plants such as *Ficus* spp, *Carica papaya*, *Ananas comosus* and *Actinidia chinensis* (Stepek et al., 2004). Other examples are tannin containing plants which have known AH activity against GIN of ruminants, particularly sheep and goats (Hoste et al., 2012).

Irrespective of the methodology used to choose which materials are selected to search for an AH effect, those materials may be used as phytotherapy and/or nutraceuticals. A phytotherapy is based on a plant, or mixture of plants, used in a similar way as a synthetic AH drug, being to cure within a short term of use and is usually administered per animal (Hoste et al., 2008). In contrast, a nutraceutical is a feed used long term for health improvement and/or maintenance, and depends on voluntary intake by the animals (*e.g.*, tannin containing forage or browse; Andlauer and Furst, 2002).

3. How to prove that a plant material has *in vitro* anthelmintic activity?

Some recent papers reviewed various *in vitro* tests to investigate antiparasitic activity against different stages of GIN, being egg hatch assay (EHA), larval feeding inhibition assay (LFIA), larval exsheathment inhibition assay (LEIA), larvae migration inhibition assay (LMIA), larval development assay (LDA) and adult motility inhibition assay (AMIA) (Hoste et al., 2008; Jackson and Hoste, 2010). The majority of *in vitro* research has been against small ruminant GIN. However we found little *in vitro* research with helminth parasites in other host species.

Even with the techniques already validated for a given parasitic species (*i.e.*, GIN of ruminants) the protocols must be adjusted for local laboratory conditions, such as the type of water and pH, temperature of the laboratory and strain of parasite studied, as it has been suggested for *in vitro* tests used to test AH efficacy (Coles et al., 2006). Also, the material tested might not be applicable to all tests.

4. How to prove that a plant material has *in vivo* anthelmintic activity?

The *in vitro* AH evidence obtained with a plant material against a stage of the life of a parasite is not sufficient to suggest direct AH effect in naturally infected animals. Thus, *in vivo* evidence is needed and the parameters to claim AH efficacy in a nutraceutical option cannot be those used for a product intended as an AH drug, such as those reported by Wood et al. (1995) for ruminants. In addition, the nutraceuticals do not need the same legal requirements and they can be commonly used as "every day" feed. However, it is important to consider aspects such as:

4.1. Biological relevance of an in vitro technique

In vitro tests used to screen materials for their AH effect might not have biological relevance for the parasites of interest in the target host. For instance, a reduction of egg hatchability of GIN in the presence of an extract is a valuable feature if the aim is to reduce pasture infectivity. However, that same material might have no effect against the worm burdens inside the host. Furthermore, when a given plant extract is screened with *in vitro* techniques, the results could show an AH effect when measured with one technique and a limited AH effect when measured with another (Alonso-Díaz et al., 2011).