Medicinal plants for helminth parasite control: facts and fiction

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The use of medicinal plants for the prevention and treatment of gastro-intestinal parasitism has its origin in ethnoveterinary medicine. Although until recently the majority of the evidence on the antiparasitic activity of medicinal plants was anecdotal and lacked scientific validity, there is currently an increasing number of controlled experimental studies that aim to verify and quantify such plant activity. There are indeed a large number of plants whose anthelmintic activity has been demonstrated under controlled experimentation, either through feeding the whole plant or administering plant extracts to parasitised hosts. However, contrary to traditional expectation, there are also a great number of plants with purported antiparasitic properties, which have not been reproduced under experimental conditions. In this paper, we discuss the source of such inconsistencies between ethnoveterinary wisdom and scientific experimentation. We focus on the strengths and weaknesses of the existing methodologies used in the controlled studies to determine the activity of antiparasitic plants. We discuss issues like the seasonal and environmental variability of the plant composition, and how this can affect their antiparasitic properties and highlight the importance of identifying the mechanisms of action of such plants and the target parasite species. In addition to their antiparasitic properties, medicinal plants may also have anti-nutritional properties, which can affect animal performance and behaviour. For this reason, we emphasise the need for considering additional dimensions when evaluating medicinal plants. We also question whether using similar criteria as those used for the evaluation of anthelmintics is the way forward. We propose that a holistic approach is required to evaluate the potential of medicinal plants in parasite control and maximise their benefits on parasitised hosts.

Keywords: bioactive plants, ethnoveterinary medicine, medicinal plants, parasites, ruminants

Introduction

For centuries, medicinal plants have been used to combat parasitism, and in many parts of the world are still used for this purpose. In ethnoveterinary medicine, which draws inspiration from traditional practice, there seems to be a range of plant/s or plant extract suitable for treating almost every parasitic disease of livestock (International Institute of Rural Reconstruction (IIRR), 1994). For example, seeds of garlic, onion and mint have been used to treat animals that suffer from gastro-intestinal parasitism, whereas extracts of the tobacco plant have been used to treat the skin of livestock afflicted with external parasites (Guarrera, 1999). Leaves, dried flowers and oil from *Chenopodium ambrosioides*, a shrub that originated from Central America and has been distributed around the world, have all been used as anthelmintics since the early 1900s (Guarrera, 1999).

Reports from around the world include exhaustive lists of plants that have been reported to have medicinal properties (Hammond *et al.*, 1997; Akhtar *et al.*, 2000; Waller *et al.*, 2001; Nundkumar and Ojewole, 2002; Athanasiadou and Kyriazakis, 2004; Fajimi and Taiwo, 2005; Githiori *et al.*, 2006).

Although the majority of the evidence on antiparasitic activity of plants has been traditionally based on anecdotal observations, there is currently an increasing number of controlled experimental studies that aim to verify, validate and quantify in a scientific manner such plant activity. Traditionally, there are two approaches that have been employed for this purpose. The first one is through offering plants or plant parts to naturally or experimentally infected animals and quantifying the consequences of their consumption. The second approach is through testing plant extracts and concoctions derived from medicinal plants via *in vitro* and *in vivo* systems. Although a number of medicinal plants have been evaluated through these methodologies and have been found to be active against

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parasites, the purported antiparasitic properties of a large variety of plants have not been reproduced under controlled experimentation. The source of such inconsistencies between ethnoveterinary wisdom and scientific experimentation is discussed in the present review. In the first part of the review, we focus on the weaknesses and strengths of the existing methodologies used to determine the antiparasitic activity of the whole plant. We discuss issues like the seasonal and environmental variability of plant composition and how this can affect their antiparasitic activity, and highlight the importance of identifying the active compounds and mechanisms of such plants and the target parasite species. In the second part, we explore the methodologies used to test the plant extracts for antiparasitic activity and question their value as a tool for this purpose. We discuss how the efficiency of medicinal plant extracts can be compromised by a variety of reasons, which include the interactions between plant secondary metabolites (PSM) and nutrients, host physiology and the site of parasitism. We conclude that in order to explore the full potential of the medicinal plants and progress towards their implementation in parasite control strategies, we need to evaluate their activity in a holistic manner and thus exploit the complementarity of all methodologies available for this purpose.

Studies on the whole plant: strengths and limitations

The emergence of resistance to anthelmintic drugs, which is now a worldwide phenomenon (Jackson and Coop, 2000), and the increased awareness of consumers about drug residues that potentially enter the food chain have stimulated investigation into alternatives to commercially available anthelmintics, such as medicinal plants. Their persistence in various environments and the wealth of information available from ethnoveterinary sources in many parts of the world has resulted in medicinal plants attracting attention from the scientific community. In an attempt to utilise as effectively as possible the information available from ethnoveterinary and medicinal reports on the anthelmintic activity of plants, there is a current trend to validate such plants under controlled experimental conditions. The variety of methodologies used for this purpose includes the provision of fresh, conserved or dried plants or plant parts to parasitised animals. For example, the consumption of leaves of wormwood in the form of powder (*Artemisia brevifolia*), one of the bitterest of plants, has been tested in a controlled study for its anthelmintic activity. Iqbal *et al.* (2004) demonstrated that the consumption of the whole plant resulted in a 62% reduction of the abomasal nematode *Haemonchus contortus* egg counts. The consumption of fagara leaves (*Zanthoxylum zanthoxyloides*), a native tree from Africa, believed to have antiparasitic activity, resulted in reduced egg excretion by the same nematode in sheep, when consumed regularly in small amounts (Hounzangbe-Adote *et al.*, 2005). Similarly, lespedeza (*Sericea lespedeza*), a grazing perennial legume

native of Eastern Asia showed promising anthelmintic activity when offered to goats either fresh (Min *et al.*, 2004) or as hay (Shaik *et al.*, 2004; Lange *et al.*, 2006). Ethnoveterinary sources from south-east Asia report that cassava forage (*Manihot esculenta*) has been used by traditional healers with success for the control of internal parasitism (Sokerya and Preston, 2003). The consumption of cassava hay resulted in lower faecal egg counts and worm burdens in sheep parasitised with abomasal and intestinal nematodes compared with unsupplemented controls (Sokerya and Preston, 2003; Bunyeth and Preston, 2006).

However, not in all cases the evidence on the antiparasitic properties of plants is consistent with the expectations arising from traditional views. The neem tree (*Azadirachta indica*) is known for its medicinal properties and has been recommended for use against gastro-intestinal nematodes and related problems in many parts of the world (Biswas *et al.*, 2002; Subapriya and Nagini, 2005). However, when leaves of the neem tree were offered to parasitised sheep, either fresh or dried, no anthelmintic effect was recorded against *H. contortus* (Githiori *et al.*, 2004; Costa *et al.*, 2006). In contrast, in another study, Chandrawathani *et al.* (2006) reported the effectiveness of neem in reducing worm numbers of the same nematode in the abomasa of small ruminants fed on fresh neem leaves on a daily basis. *Melia azederach*, another plant that belongs to the same family as the neem tree, has also been reported to have anthelmintic activity. However, under controlled experiments, no anthelmintic activity has been demonstrated (Hordegen *et al.*, 2003). In addition, there is a large number of grazing forages, including *Lotus pedunculatus* and *Hedysarum coronarium*, whose anthelmintic activity has been shown to be rather inconsistent across the various studies around the world (Niezen *et al.*, 1998; Garcia *et al.*, 2003; Marley *et al.*, 2003; Athanasiadou *et al.*, 2005; Tzamaloukas *et al.*, 2005).

The interpretation of the observed inconsistencies in the activity of medicinal plants when offered to parasitised animals, either as a supplement or single food, is not straightforward. In cases where evidence is anecdotal, one part of the problem seems to be the misinterpretation of facts in various communities, often due to the lack of scientific knowledge. For example, traditional healers are not always familiar with the parasite species that are most pathogenic for livestock. In a participatory study in northern Kenya, traditional healers identified plants as being very effective antiparasitics if they expelled tapeworm segments (Githiori *et al.*, 2004). The latter are easy to identify, as they are visible with the naked eye, but not as pathogenic as helminth nematodes, whose both parasitic and non-parasitic stages require specialised knowledge and equipment to be identified. Thus, in some cases, plants may have been mistakenly included in lists with those reported with anthelmintic properties and these mistakes may be justified when controlled experimentation is performed.

In other cases, the inconsistencies observed might be related to methodological limitations while testing the

anthelmintic properties of medicinal plants. For example, testing such plants in rodent and other models might not always be appropriate. The majority of ethnoveterinary reports originate from ruminants, as the main livestock species that generate income in poor countries (IIRR, 1994). Consequently, when the antiparasitic activity of such plants is tested in rodent models, for example in the form of dried plant, part of the reported variation may be due to the physiological difference between ruminant and non-ruminant animals (Satrija *et al.*, 1994; Ignacio *et al.*, 2001; Githiori *et al.*, 2003a and 2003b). Other methodological limitations include the great variation observed in the protocols of collection and storage of the plant material prior to its use, if not grazed or consumed immediately. The latter will result in changes in plant availability in nutrients and metabolites, which may affect the reproducibility of their anthelmintic activity. For example, in the above study by Chandrawathani *et al.* (2006) on the neem tree, the leaves were reportedly collected daily and fed fresh to the animals, whereas Githiori *et al.* (2004) fed conserved leaves. The observed inconsistency on the anthelmintic effects of neem tree in the above studies could be attributed to the method of preservation, which may have affected the plant properties. In most of the cases, the antiparasitic properties of plants are exerted through PSM. These metabolites are unstable molecules and their biological activity will be dependent on their structure and physical and chemical properties (Waterman, 1988 and 1992). Variable conditions of collection and storage of the plants have been shown to affect these properties and likely their anthelmintic activity as well. In addition, seasonal and environmental variability will have an impact on the synthetic pathways of the PSM, which can potentially affect their physical and chemical properties (Mueller-Harvey and McAllan, 1992).

Prior to considering incorporating medicinal plants in parasite control schemes, the scientific community should provide strong evidence on their benefits on parasitised hosts and address the issue of inconsistency across the studies around the world. We believe that in order to minimise the inconsistencies reported and maximise the repeatability of the results, there is an urgent requirement for the development and utilisation of a standardised methodology for the evaluation of their activity around the world. There is no system currently available to sufficiently characterise the plants in terms of their anthelmintic properties, quantify the latter and finally standardise their use for parasite control in different parts of the world. Such a system could be used as a common currency from scientists around the world to describe the anthelmintic potential of bioactive plants. A first step towards achieving this would be the identification of active compounds in medicinal plants. Subsequently, this information could be used to characterise the medicinal plants by estimating their content in the active compound. This would enable comparisons to be made on the same basis across studies and will also explain the variability of the results.

We further exploit this by taking the inconsistency related to neem tree as an example.

Although the active compound(s) in the neem tree has not yet been isolated, its high content in condensed tannins has led towards hypothesising that these polyphenolic compounds might be responsible for its anthelmintic activity. Possibly due to cost implications and design limitations, condensed tannin content and plant description was not included in any of the studies previously mentioned (Chandrawathani *et al.*, 2002 and 2006; Githiori *et al.*, 2004; Costa *et al.*, 2006). This would have helped towards accounting for the potential inconsistencies among the different studies. As the process of isolating the active compounds is long, complex, and often requires specialised equipment, bibliographic evidence on the active compounds and subsequent determination of their concentration in the plant would also be useful. Admittedly, this process can be complicated in cases where the anthelmintic activity of a plant is attributed to more than one compounds. Furthermore, the bioavailability of the active compound in the host is not always directly related to the concentration in the plant, as will be explained in the next part. We still however believe that there is a requirement for the use of a common currency among scientists, in a form of a plant-compound database or index, which will provide a solid reference system used globally. Such a tool, which would need to be the outcome of an interdisciplinary collaboration, should enable scientists to quickly screen medicinal plants by measuring concentrations of the active compound and consequently evaluate its anthelmintic potential.

In the next section, we describe the advantages and pitfalls of the second methodology often used to evaluate the anthelmintic properties of medicinal plants. Although some of the issues raised above apply for this second methodology as well, for the purpose of clarity they will not be further addressed in the next section.

Extracts: is their use the way forward in the validation of medicinal plants?

The effects that parasitised hosts experience as a consequence of plant consumption result from interactions between the nutritional values and the pharmacological/ medicinal properties of the plants. In order to facilitate the validation process of the medicinal plants and address some of the methodological drawbacks mentioned in the previous section, there is a concurrent trend towards using plant extracts to assess the anthelmintic activity of medicinal plants. Extraction procedures used for this purpose vary from simple water extractions to very complicated ones, where a series of organic solvents is used (Waterman and Mole, 1994). The aim is to extract the active compounds from the medicinal plants, and then test their anthelmintic activity, through *in vitro* and *in vivo* systems. The anthelmintic properties of several medicinal plant extracts have been evaluated through *in vitro* systems and their efficiencies have in some cases approached 100% (Satou *et al.*,

2002; Molan *et al.*, 2003a; Ademola and Idowu, 2006). In addition, *in vivo* studies have shown that the administration of quebracho extract, a commercially available extract from *Schinopsis* spp., reduced faecal egg counts and worm numbers in parasitised sheep (Athanasiadou *et al.*, 2001a; Butter *et al.*, 2001). Similarly, parasitised goats benefited from the inclusion of plant extracts containing high levels of secondary metabolites in their diets (Akhtar and Ahmad, 1992; Paolini *et al.*, 2003a and 2003b). In some cases, the antiparasitic efficacy of plant extracts has been similar to that of broad-spectrum anthelmintic drugs; Satrija *et al.* (1994) almost eliminated intestinal nematodes within 7 days of supplementation with papain extract.

However, not in all cases the alleged anthelmintic activity of certain plant extracts, as reported by ethnoveterinary reports, was confirmed by controlled experimentation. For example, the administration of plant extracts used in Kenya by herbalists in parasitised sheep did not reduce the level of parasitism in controlled experimental studies (Githiori *et al.*, 2002). In other cases, although some degree of reduction was observed, this was considered not to be of major importance for their use in parasite control (Githiori *et al.*, 2003b). The oil of *C. ambrosioides* has been known for centuries for its anthelmintic properties. It was included in the British Veterinary Codex until the middle of last century (1953) and is reported for anthelmintic activity in scientific reviews (Tagboto and Townson, 2001; Waller *et al.*, 2001). However, when tested under controlled conditions against abomasal nematodes, no anthelmintic activity was reported (Ketzis *et al.*, 2002). Inconsistency is observed not only between ethnoveterinary and scientific reports but also across scientific experiments. The administration of quebracho extract (see above) resulted in a reduction in the abomasal worm burden in one case (Max *et al.*, 2005), whereas only the intestinal worm burden was affected in another case (Athanasiadou *et al.*, 2001a).

One of the challenges we are faced with, when using plant extracts to assess the anthelmintic activity of medicinal plants, is relating the concentration of the active compound in the extract and that found in the plant. The plant extract, as obtained following the extraction process, will inevitably have a high concentration of the active compounds. In most cases, this will not correspond to the concentration of the active compounds consumed by parasitised hosts when the plant is included in their diets (Molan *et al.*, 2003a). As a consequence, it is not uncommon to observe high anthelmintic efficacy of medicinal plants when their extracts are tested *in vitro* (Athanasiadou *et al.*, 2001a; Ketzis *et al.*, 2002; Paolini *et al.*, 2004; Barrau *et al.*, 2005) or when offered as a medicinal supplement (Athanasiadou *et al.*, 2001a; Butter *et al.*, 2001). However, efficacy is not near as high when whole plants are offered to parasitised hosts (Niezen *et al.*, 1998 and 2002; Tzamaloukas *et al.*, 2005). Furthermore, *in vitro* models are often used to validate plant extracts, without the simultaneous use of *in vivo* experimentation. Although *in vitro* testing of the antiparasitic properties plant extracts offers

the opportunity to screen large numbers of plant extracts at low cost and rapid turnover, *in vitro* results are not always verified by *in vivo* experimentation, and it is often questionable whether the *in vitro* assays are relevant to *in vivo* conditions (Athanasiadou and Kyriazakis, 2004). The great variety of models and methods available to test the anthelmintic properties of plants and the lack of measures to minimise experimental variability contribute towards an increased apparent conflict of evidence regarding the anthelmintic properties of plant extracts.

Furthermore, other issues, such as the bioavailability of the active compounds at different parts of the gastrointestinal tract, the host–plant interactions and the parasite specificity also increase the degree of variability observed in these studies. It has been shown that it is highly likely that certain plants are more active against specific parasite species than others (Athanasiadou *et al.*, 2005; Tzamaloukas *et al.*, 2005). This might be related to the parasite niche or the bioavailability of the compound in the different compartments of the gastro-intestinal tract of the parasitised host. Condensed tannins, for example, have been shown to form complexes with macromolecules, such as proteins (Mueller-Harvey, 2006). Due to physiological conditions, tannins are expected to be in complexes in the abomasa of parasitised hosts. When in complexes, they are likely unavailable to exert their anthelmintic activity; this could be why abomasal nematodes were not affected *in vivo* by condensed tannins, whereas they were affected in an *in vitro* system (Athanasiadou *et al.*, 2001a). The protein–tannin complexes are expected to be disassociated in the small intestine, and thus extracts rich in condensed tannins were effective against intestinal parasites. However, when hosts are offered a diet rich in protein, tannins may remain in complexes with the protein in the small intestine, and thus lower their anthelmintic efficacy (Athanasiadou *et al.*, 2001b). Compound bioavailability and thus efficacy of medicinal plants may also be related to the host species. For example, although the ingestion of condensed tannins did not affect the abomasal worm burden in sheep, it did in goats (Paolini *et al.*, 2003a). It is known that a number of physiological adaptations have taken place in the gastro-intestinal tract of goats, in comparison to that of sheep, to counteract the presence of secondary metabolites in the browse material. It has been hypothesised that such differences might be responsible for the host species specificity often observed in the anthelmintic activity of condensed tannins (Hoste *et al.*, 2006).

Identifying the active compounds in plant extracts, as described in the previous section, quantifying them in the plant and estimating their bioavailability in the host are essential steps towards strengthening the evidence of the anthelmintic activity of medicinal plants through reducing the inconsistency of the evidence. This is a prerequisite towards achieving the scientific validation of plants for parasite control. It will also contribute towards improving our understanding on host–parasite–compounds interactions in order to consider ways of further increasing the

efficacy of such compounds and ensure their best possible use for parasite control. It is imperative that effort is directed towards identifying active plant compounds for another reason: the active compounds contained in the medicinal plants are often responsible for a variety of negative side effects on the parasitised host. We will briefly address this issue below, as it has recently been reviewed elsewhere (Athanasiadou and Kyriazakis, 2004; Hutchings et al., 2006) and then propose the approach required to exploit medicinal plants to their full potential.

Medicinal plants and parasitised hosts: viewing the whole picture

Although the majority of compounds with anthelmintic properties have yet to be isolated from forages and plants, in most cases such compounds have been identified, they are PSM. For example, lactones, such as santonin isolated from *A. maritima*, have shown a strong anthelmintic activity towards *Ascaris* spp., nematode species of livestock and humans (Waller et al., 2001). Alkaloids have also demonstrated strong nematocidal activity towards *Strongyloides ratti* and *S. venezuelensis*, two rat nematodes used as models for human nematodes (Satou et al., 2002). The nematocidal activity of tannin extracts has been reported as early as the 1960s (Taylor and Murant, 1966), and more recently evidence on the anthelmintic properties of condensed tannins has been supported by a series of *in vitro* (Dawson et al., 1999; Athanasiadou et al., 2001a; Molan et al., 2003b; Ademola and Idowu, 2006) and *in vivo* studies (Athanasiadou et al., 2000; Butter et al., 2001; Paolini et al., 2003a and 2003b). However, despite their anthelmintic properties, it is not yet clear whether medicinal plants could actually have a role in controlling parasitism in livestock. This is because the consumption of medicinal plants either in form of plant parts or as extracts has also been related to the demonstration of toxic effects on hosts. These detrimental effects are often attributed to the same plant metabolites that are responsible for the anthelmintic effects. Alkaloids, terpenes, saponins, lactones, glycosides and phenolic compounds are classes of active plant metabolites whose excessive consumption can detrimentally affect herbivore health and in extreme cases, survival. For example, the excessive consumption of tannins, which are polyphenolic compounds, has been associated with a reduction of food intake and food digestibility, impairment of rumen metabolism and mucosal toxicity (Hagerman and Butler, 1991; Rittner and Reed, 1992; Reed, 1995; Dawson et al., 1999). Saponins, which are terpenoids, have been considered responsible for reducing food intake, causing nutritional deficiencies, haemolysis and in extreme cases death of herbivores (Applebaum and Birk, 1979; Milgate and Roberts, 1995). Excessive consumption of cyanogenic glycosides, terpenes or alkaloids can result in neurological defects (Conn, 1979). Cysteine proteinases were highly toxic, despite their obvious anthelmintic activity (De Amorin et al., 1999; Stepek et al., 2005 and 2006).

Despite the abundant evidence on the potential negative effects of plant active metabolites in herbivores, to date the majority of the studies investigating the anthelmintic activity of medicinal plants is lacking measurements on the potential negative effects on the host. A small number of studies have monitored host's performance (Athanasiadou et al., 2000 and 2001a; Butter et al., 2001; Githiori et al., 2004), and have reported clinical toxicity (Akhtar and Ahmad, 1992; Satrija et al., 1994; Dawson et al., 1999; Githiori et al., 2003a), which escalate as the concentrations of active compounds increase. In extreme cases, even the death of animals under treatment has been reported (Athanasiadou et al., 2001a; Githiori et al., 2003a). For parasitised animals to benefit from the anthelmintic properties of the medicinal plants, the antiparasitic effects should outweigh their antinutritional consequences on the performance of the parasitised host. The latter will depend greatly on the severity of the consequences towards the host on the one hand and towards the parasite on the other hand, as it has been discussed in two recent reviews (Houdijk and Athanasiadou, 2003; Athanasiadou and Kyriazakis, 2004). Parasitised hosts might even be able to tolerate short-term negative consequences (e.g. toxicity) if they are to attain long-term benefits (e.g. parasite reduction; Kyriazakis and Emmans, 1992).

In addition to the detrimental effects of plant compounds on the performance, their consequences on behaviour of parasitised hosts is yet another aspect that we believe needs to be considered, in a similar manner as performance. This is an essential issue as there is evidence from rodent models suggesting that the administration of plant extracts may result in a range of either positive (Herrera-Ruiz et al., 2006; Pultrini et al., 2006) or negative effects (Franco et al., 2005) on the behaviour of parasitised hosts. Changes in the behaviour of hosts, for example the introduction of behaviour that may be considered stereotypic as an outcome of the plant administration, may result in significant costs on the host's welfare status. Combating parasitism *per se*, but at the same time introducing behaviours that are considered indicative of poor welfare, would not be a desirable side effect of medicinal plant administration.

However, it is not just the antiparasitic and antinutritional effects of medicinal plants that should be taken into account when considering their use for parasite control. An emerging aspect of the potential benefits of medicinal plants is their contribution towards the development of host resistance to parasites. There is recent evidence suggesting that the consumption of medicinal plants or plant extracts has improved the immune response of parasitised hosts, by increasing the number of specific effector cells (Huffman et al., 1997; Niezen et al., 2002; Tzamaloukas et al., 2006). Consequently, in addition to the antiparasitic and antinutritional effects of medicinal plants on host performance and behaviour, the immunomodulatory effects of plants are another benefit of the consumption of medicinal plants. To date, all such effects of medicinal plants have been mostly described in response to parasites. The possibility that the

improvement in the immunity is generic, which would offer an added benefit to the well being of the host, cannot be disregarded and requires further investigation.

There is currently a lot of controversy surrounding the evaluation of the activity and the role of medicinal plants for parasite control. Parasitologists have recommended that threshold points should be established, below which the efficacy of medicinal plants for parasite control should not be considered. It has been suggested that such threshold points should be similar to those set for commercial anthelmintics (Vercruysse and Claerebout, 2001). However, because of the various different aspects that need to be considered to justify the use of medicinal plants for parasite control, as these have been discussed above, it is disputable whether we should have the same set of criteria as those used for the evaluation of the anthelmintics. It has recently been suggested that rather than evaluating the anthelmintic efficacy of plant extracts *per se*, it would be more acceptable to justify their use based on the economic threshold on efficacy (Ketzis *et al.*, 2006). We are in agreement with this view; when considering medicinal plants, it is sensible to estimate the overall benefit or the cost of their use at all different levels, prior of making the evaluation of their applicability. We should be looking for evidence whether the use of medicinal plants can improve the resilience/resistance of hosts, their well-being and the production level. We should also be looking at indicators of sustainability of their anthelmintic activity prior incorporating medicinal plants in parasite control. Currently, there is no

published evidence on the development of resistance to any type of medicinal plants. It is possible that due to the lower anthelmintic efficiency of plants compared with the anthelmintic drugs, selection pressure on the resistant parasite population is not strong. Alternatively, anthelmintic drugs seem to be carrying out their anthelmintic activity by influencing a single mechanism in the parasite (Geary, 2005), whereas plant compounds may demonstrate a variety of effects, as discussed earlier. Consequently, the expectation would be that resistance will develop at lower rates, compared with anthelmintics, if developed at all. Generation of evidence on the mechanisms of action of specific compounds will contribute towards making safe assumptions on the development of resistance to medicinal plants.

Conclusions

Methodological shortcomings in the various approaches used to describe the anthelmintic properties of medicinal plants have led to the debate about the consistency of their activity and thus their potential use for parasite control. We believe that progress can be achieved by considering the various aspects of medicinal plants together and thus exploit their complementarity. Without a doubt, coordinated effort should be directed towards the experimental validation of plants with medicinal properties deriving from ethnoveterinary sources. Table 1 lists the most common misconceptions and the facts related to the anthelmintic

Table 1 *Popular beliefs, facts and action required to exploit the medicinal plants and their anthelmintic properties to their full potential*

Beliefs	Fact	Action proposed
All medicinal plants have anthelmintic properties	Some medicinal plants have anthelmintic properties	Screen plants through *in vitro* and *in vivo* models
Ethnoveterinary sources are always accurate	Some of these may be accurate	Use ethnoveterinary reports with caution; confirm with controlled experimental studies
All medicinal plants will directly kill the parasites	Medicinal plants may improve the resistance and/or resilience of the parasitised host	(1) Monitor performance and behaviour of parasitised hosts. (2) Monitor local and systemic immune responses
Medicinal plants are safe to ingest	Excessive consumption of some medicinal plants may be toxic	Monitor host's health and performance during the experiments.
The activity of the medicinal plants is consistent	Different plant content results in variable anthelmintic activity	(1) Monitor activity in various environments. (2) Identify the active compounds. (3) Calculate bioavailability. (4) Standardise methodologies
Medicinal plants are only found in tropical countries	Maybe available also in temperate climates	Review appropriate literature; less well known in temperate climates due to abundance of conventional medicine
If it works *in vitro*, it should work *in vivo*	Different conditions/concentration of the active compounds. Synergistic/antagonistic effects between compounds	(1) Combine both types of experimentation and test all possible extracts from each plant. (2) Consider bioavailability of compounds
If it works in one host species or for one parasite species it will work for all	Some plants will work for some parasites/in certain hosts due to variable bioavailability	(1) Conduct experiment in many species. (2) Host–parasite specificity
Expelled worms are always visible after plant ingestion	The species expelled may not always be pathological to the host or may not be visible	Train people to recognise the economically important species of parasites
The method of preparation used traditionally is the best	There are variations in activity depending on methodologies used to prepare the extracts	(1) Identify active compound for each plant species. (2) Take into account the bioavailability of the compound

activity of the medicinal plants. Action is required to achieve reproducible evidence on their anthelmintic activity and thus have it appreciated by the worldwide scientific community. We emphasise the need for incorporating additional measurements on ongoing research, such as performance measurements, indicators of immunity and behavioural observations when considering the potential of such plants. This will lead to a more holistic investigation to the properties of plants with antiparasitic properties and influence their potential exploitation in livestock systems.

Acknowledgements

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