Plant-Based Solutions to Global Livestock Anthelmintic Resistance

Katherine E. French

Abstract Anthelmintic resistance in livestock is increasing globally. Livestock intestinal parasites now develop resistance to synthetic anthelmintics within 2–10 years, collectively costing billions of dollars annually in lost revenue around the world. Over-reliance on commercial drugs and dips and changes in livestock management practices are key drivers of this trend. To date, current research has focused on identifying new anthelmintics from bacterial and fungal sources or even synthesizing new drugs that target parasite metabolism or reproduction. Plant-derived anthelmintics are a promising alternative, yet to date major research funders and scientists have overlooked this option. Until the mid-20th century, rural communities relied on plant-based methods of controlling livestock parasites. These methods include feeding livestock specific medicinal plants and trees, grazing livestock on herbal leys, and changing where livestock grazed based on ecological factors (e.g., flooding) that increased parasite burdens. Many historic texts and ethnological accounts record the ethnobotanical knowledge of rural communities and the plants they used to control livestock intestinal parasites. Some traditions persist today yet the farmers, graziers, and shepherds who hold this knowledge are rapidly disappearing and with them perhaps a potential long-term solution to anthelmintic resistance. This short perspective piece will cover recent research using ethnobotanical data as a means to identifying potential new anthelmintics; the morphological, physiological, and metabolic effect of plant secondary metabolites on parasites; and an overview of “best practices” which can reduce bias in assessments of plant bioactivity and increase reproducibility of test results. This will hopefully bring recent advances in ethnobiology, chemistry, and ecology to new audiences, and, potentially, spark new interest in using medicinal plants to improve livestock health.

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Keywords Drug-resistance, Livestock, Local ecological knowledge, Conservation, Ecology

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Introduction Anthelmintic resistance in livestock is increasing globally. In the USA, South America, and South Africa, current pharmaceutical anthelmintics (e.g., benzimidazoles, avermectins) are now completely ineffective in many regions (Kaplan and Vidyashankar 2012; Shalaby 2013; Vatta and Lindberg 2006). In the UK and northern Europe resistance is also on the rise, but complete resistance has yet to occur (Taylor et al. 2009; Traversa and von Samson-Himmelstjerna 2016). Climate change and global trade have also increased helminthic infections in livestock by increasing the abundance of specific zoonotic parasites (or their hosts), and by introducing new parasites into new regions (Fayer 2000; Fox et al. 2011; Karesh et al. 2012; Patz et al. 2000; Semenza and Menne 2009). Anthelmintic resistant parasites affecting livestock can also spread to humans (e.g., through hybridization of parasites affecting livestock and those affecting humans, as in the case of schistosomiasis and fascioliasis), leading to billions of dollars in economic loss and thousands of human lives every year (King et al. 2015; Waller 2006). This is particularly severe in developing countries due to over-use/misuse of anthelmintics, poor sanitary conditions, and shared land and water use among livestock and humans (King et al. 2015). The use of synthetic anthelmintics also has wider ecological and economic effects. Synthetic anthelmintics reduce soil invertebrate diversity (Spratt 1997; Strong 1993). For
example, lab and field studies suggest anthelmintic residues in livestock dung reduce beetle populations by decreasing egg production and increasing larval mortality (Cook et al. 2017; Numa et al. 2012; Ridsdill-Smith 1993). International and national initiatives support the development of new preventative or therapeutic alternatives, but current research continues to focus on developing chemical solutions that deactivate specific genes or proteins in parasites that disrupt ability to feed, nicotinic acetylcholine receptors (nAChR), and fertility (Hotze et al. 2010; Kaminsky et al. 2008; Sabatelli 2010).

Exploiting the diversity and bioactivity of plant secondary metabolites may be a viable alternative. Plants naturally produce over 60,000 chemical compounds to deter herbivores, to destroy microbial pathogens, and to communicate with other organisms like pollinators (Wink 2010). Before the creation of synthetic anthelmintics by drug companies in the mid-20th century, humans relied on plants to control livestock intestinal parasites (Corley and Godley 2011). In Europe, medieval herbals and 17th–19th century printed books are filled with descriptions of plants fed to livestock to expel parasites. Today, many small farmers and pastoralists around the world continue to use plants to treat livestock diseases. For example, in South Africa aloes are the premier anthelmintic (Beinart and Brown 2013). In northern Europe, small farmers still value old “traditional” pastures rich in medicinal herbs and legumes for the perceived anthelmintic qualities of specific wild plants (French 2017). Because many of these plants are actively consumed by livestock within traditional agropastoral systems, their toxicity and environmental effects are likely low.

Yet these traditions are rapidly disappearing and with them perhaps a potential long-term solution to anthelmintic resistance. This short perspective piece will cover recent research using ethnobotanical data as a means to identify potential new anthelmintics; the morphological, physiological, and metabolic effect of plant secondary metabolites on parasites; and an overview of “best practices” which can reduce bias in assessments of plant bioactivity and increase reproducibility of test results. This will hopefully bring recent advances in ethnobiology, chemistry, and ecology to new audiences, and, potentially, spark new interest in using medicinal plants to improve livestock health.

**Phyto-Anthelmintics: Old Plants, New Leads**

Over the past ten years the number of publications on plants used to treat livestock parasites has doubled (Figure 1). An increasing resistance to traditional synthetic anthelmintics may be responsible. The majority of these publications are from India, although there are a surprising amount of publications from the US and UK. Most research is published in the journals relating to parasitology, pharmacology, veterinary sciences, and plant sciences. A phytochemical database run by the United States Department of Agriculture (USDA) contains 1,029 plants with 58 different chemicals with anthelmintic properties (United States Department of Agriculture 1992-1996) (Supplementary Materials Table 1). The top five plants with the highest number of anthelmintic compounds are *Achillea millefolium*, *Dryopteris filix-mas*, *Pennisetum boldus*, *Rosmarinus officinalis*, and *Salvia officinalis*. Although the database contains plants from all around the world, the majority of these are cultivated or economic plants and many wild plants (even common ones) are excluded. For example, many wild legumes found in British meadows (e.g., *Lathyrus pratensis*, *Vicia cracca*) are absent. In addition, many indigenous plants recently evaluated for anthelmintic qualities are not found in the database. One solution would either be to actively maintain this phytochemical database by allowing users to upload data, or to create a new open-access database specifically for anthelmintic plants.

Perhaps one of the most surprising aspects of anthelmintic plants is that they are often common (Figure 2). For example, Bartha et al. (2015) found that villagers in Romania used *Allium sativum* bulbs, *Cucurbita pepo* seeds, *Daucus carota* ssp. *sativus* roots, and *Quercus petraea* and *Quercus robur* nuts to treat pigs, cattle, and horses. Similarly, in northern Europe many of the plants reported by farmers and pastoralists to have anthelmintic properties are wild plants commonly growing in pastures and meadows (Waller et al. 2001). In addition, a number of studies have shown that the bark, fruits, and nuts of many trees found in traditional rangeland and pasture systems and which are naturally consumed when livestock are ill (zoopharmacognosy) have anthelmintic properties. For example, many of the plants found in arid rangelands of Jordan contain plants such as *Achillea fragrantissima* (Lavender cotton), *Artemisia judaica* (wormwood), and *Thymus horei*, which have anti-parasitic properties according to Bedouins (Al-Tabini...
In British Columbia (Canada), *Juniperus communis* (juniper), *Pinus ponderosa* (Pinaceae) (yellow pine), and *Symphoricarpos albus* var. *laevigatus* (snow berry) branches are used against endoparasites and liver fluke (Lans et al. 2007). The same plants (or another from the same genus) are also used as anthelmintics in geographically dispersed regions. For example, juniper is used to treat liver fluke in Canada, as mentioned above, while the leaves of *Juniperus excelsa* are used by the Wakhi pastoralists of Afghanistan (Soelberg and Jäger 2016). Other anthelmintic plants with widespread, cross-cultural use include: *Urtica dioica* (nettle), *Mentha pulegium* (pennyroyal), *Digitaria abyssinica* (couch grass), *Salix* spp., and *Carica papaya* (pawpaw) (Nabkenya et al. 2014).

Ethnobotanical research can contribute to the identification of which plants might contain...
anthelmintic properties, as well as how they are prepared. This local knowledge is a form of metadata: time of collection, method of preparation, and dose can direct metabolomic, pharmacological, and epidemiological research (Silva et al. 2014). However, this knowledge is a finite resource. The widespread use of synthetic anthelmintics has spurred the decline of traditional anthelmintics in livestock management around the world in favor of feeds such as maize, soy, and cereals which increase daily live weight gain (Bartha et al. 2015). Farmers who switch from raising local breeds to crossed/exotic livestock breeds and/or increase herd sizes due to governmental incentives also switch from local ethnoveterinary medicines to pharmaceutical alternatives (Nabukenya et al. 2014; Vatta and Lindberg 2006). Decreased medicinal plant availability due to environmental changes or restricted access to natural sources (e.g., by limiting grazing rights) have also contributed to this change (Beinart and Brown 2013; Nabukenya et al. 2014).

**How Phytochemicals Affect Parasites**

Ethnobotanical data serve as a guide, but not a basis, for plant-based anthelmintic research. Without further chemical analyses and *in vitro* and *in vivo* tests, these data remain “hearsay”. Advances in chemical identification using multiple methods from mass spectrometry (liquid-chromatography mass spectrometry, gas-chromatography mass spectrometry) can aid in identifying the secondary metabolites found in medicinal plants. It can also lead to the discovery of new molecules that could serve as drug leads.

Research within the past ten years suggests that plants with anthelmintic properties affect multiple morphological, physiological, and metabolic targets. Plant secondary metabolites with anthelmintic

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**Figure 2** Plants Rich in Anthelmintic Compounds. Plants store anthelmintic compounds in vacuoles, resin ducts, and trichomes (phytoanticipins) and produce other compounds in response to pathogenic attack (phytoalexins). To date, plants with the greatest number of anthelmintic compounds are common, widespread, and thus, highly studied. From left to right: (A) Salvia officinalis (B) Rosmarinus officinalis (C) Achillea millefolium (D) Dryopteris filix-mas and (E) Peumus boldus. All images are available in the Public Domain (CC0).
properties reduce motility, create epidermal lesions, degrade esophagus and gut tissues, decrease egg production in females, inhibit eggs from transforming into larvae, and cause death within 24–72 hours (see Table 1). Of all the plant secondary metabolites, phenolic compounds show the highest level of bioactivity against parasitic worms. Phenolic compounds inhibit proteins and include flavonoids, coumarins, and condensed tannins (Wink and Schimmer 2010). Condensed tannins have received the most attention, and international research programs such as the EU-wide Legume-Plus initiative have sought to develop new breeds of tannin-enriched lucerne and sainfoin (http://legumeplus.eu/). However, feeding livestock tannin-dense feeds (>7% dry matter) can have detrimental effects including reduced growth rate (Hoste et al. 2006). In addition, lucerne contains phytoestrogens (coumestans) which can reduce livestock fertility (Smith et al. 1979). Lucerne and sainfoin seeds are also expensive and the latter requires fertile, moist calcareous soils to grow. These factors may limit the geographic range and farmer uptake of these plants. Selecting a range of plants with different anthelmintic bioactive compounds, instead of one or two, could be a more effective strategy to control livestock parasites. This approach would also satisfy the other dietary needs of livestock (e.g., sugar, protein, fiber, and macro and micro minerals).

The synergy of metabolites found in any given plant, and those found among plants in complex mixtures, may be more effective together than when purified, isolated, and tested on their own in vitro and in vivo. A recent ethnoveterinary study reported that 70% of all practices in the study area relied on more than one plant (Bartha et al. 2015). For example, the metabolites in Table 1 each target different parts of helminth physiology and/or reproductive cycle. However, to date no study has established whether the efficacy of anthelmintic plants is due to multiple phytochemicals working together. Statistical approaches developed to assess the activity of multi-drug therapies in cancer research could be used to determine synergistic activity. For example, the “MixLow” method combines: (1) multiple nonlinear mixed-effects models, (2) the Lowe Index, and (3) confidence intervals for the Lowe Index to investigate drug interactions (Boik et al. 2008).

The potential synergistic efficacy of plant secondary metabolites differs remarkably from current anthelmintics under development (Table 2). Current
synthetic anthelmintics target particular DNA regions, proteins, or biosynthetic pathways (e.g., chokepoints) using synthetic chemicals, proteins from other parasites, or metabolites produced by bacteria and fungi. However, the problem with all of these approaches is the specificity of the anthelmintic under development. By focusing on one target, anthelmintic resistance will continue as parasites evolve and evade current drugs. How rapidly this resistance occurs varies: some studies report resistance in 10 years, while more recent studies have reported resistance to the newest anthelmintics within 2 years (Buckingham et al. 2014). Hotspots of resistance may also emerge in areas where anthelmintics are used heavily (e.g., multiple doses per year) and for both humans and livestock (King et al. 2015).

Although many studies report the efficacy of plant-based anthelmintics in vitro and in vivo, the negative results reported from experimental research should also lend a word of caution. For example, Githiori et al. (2003) tested seven local plants used to treat anthelmintic infections in Kenya and found that only one (Ananas comosus) had weak in vitro activity. In addition, a recent study found that when goats and kids were fed a commercial herbal feed supplement containing a mix of several herbs traditionally used as vermifuges (Artemisia absinthium (wormwood), Allium sativum (garlic), Juglans nigra (black walnut), Cucurbita pepo (field pumpkin), Artemisia vulgaris (mugwort), Foeniculum vulgare (fennel), Hyssopus officinalis (hyssop), and Thymus vulgaris (thyme)) at a dose of 19 g for three days, the supplement failed to control intestinal parasites (Burke et al. 2009). This suggests that other factors, including amount of plant consumed (dose and length of administration), the effects of manufacturing and packaging, and even metabolite stability may influence the bioactivity of such supplements.

**Developing Best Practices**

Many studies on the anthelmintic properties of plants use very different methodological procedures. Different practices—from the initial collection of plant material, to method of metabolite extraction, to assay-design—can introduce bias (of false positive or false negative results). The following provides some suggestions for “best practices” which can help standardize the evaluation of plant bioactivity and increase reproducibility.

1. **Preparation of Plant Material:** Plants should be collected at the same time of day (if collected over an extended period) and dried outside in the shade or indoors in a drying room for 48 hours to one week. If plants are collected for metabolomic analysis, at least 4 replicates of each plant from each site are needed. Alternatively, freezing plants in liquid nitrogen (in Falcon tubes) followed by lyophilization as soon as plants are collected will preserve the metabolite composition (Asami et al. 2003; de Torres et al. 2010). In addition, plants prepared in this way are easier to homogenize into a fine powder which will increase the exposure of plant cell walls to the solvent of choice. Although oven drying is widely practiced, this can lead to loss of aromatic metabolites (e.g., terpenes).

2. **Assay Selection:** Agar and broth dilution assays can be used to establish the Minimal Inhibitory Concentration (MIC) and Lethal Concentration (LC) values of a crude extract on helminths. In agar assays, a petri dish is seeded with nematodes and E. coli (their food source) and then exposed to a plant extract. However, many metabolites (e.g., essential oils) do not travel through agar very well which may lead to false negatives. In broth dilution assays, 96-well microtiter plates are filled with a nematode growth medium, nematodes (e.g., 10–50 L-4 stage adults), and the crude extract under assessment (Garvis et al. 2009). The advantages of the 96-well plates are that many compounds can be assayed against nematodes in different life stages (e.g., eggs, larvae, adults) at once and the system can be semi-automated. Screening parasites at different life stages can nuances our understanding of how these plant compounds work; some might be effective at halting egg production, while others interfere with larvae growth and development. A COPAS Biosorter can be used to distribute a specific number of nematodes at a given life-stage into each well in a matter of seconds. Identification of nematode survival can be established by counting under a microscope. This process can be automated using the WormAssay protocol, where a high definition camera is attached to an inverted microscope to detect parasite motility and the captured images are analyzed using specially-designed algorithms (Marcellino et al. 2012; Storey et al. 2014). When feasible, using the latter method will provide more accurate, reproducible results.

3. **Fractionation:** Fractionation takes a specific amount of plant material and extracts metabolites...
Table 2 Non-plant based anthelmintics. Current anthelmintics are synthesized from specific lead chemicals, microbial metabolites, or parasitic worms and their activity is based on one specific target.

<table>
<thead>
<tr>
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<th>Source</th>
<th>Active Agent</th>
<th>Target</th>
<th>Reference</th>
</tr>
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<tbody>
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<td>Chemical</td>
<td>1-dimethyl-4-phenylpiperazinium (DMPP)</td>
<td>synthetic chemical</td>
<td>nicotinic agonist</td>
<td>(Kaminsky et al. 2008)</td>
</tr>
<tr>
<td></td>
<td>Albendazole</td>
<td>synthetic chemical</td>
<td>eggs</td>
<td>(Taylor et al. 2013)</td>
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<tr>
<td></td>
<td>Amino-acid derivatives (AAD)</td>
<td>synthetic chemical</td>
<td>nematode-specific clade of acetylcholine receptor subunits affecting movement, growth and viability</td>
<td>(Kaminsky et al. 2008)</td>
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<td></td>
<td>Benimidazoles</td>
<td>synthetic chemical</td>
<td>α- and β-tubulin monomers</td>
<td>(Demeler et al. 2013)</td>
</tr>
<tr>
<td></td>
<td>Dasatinib</td>
<td>synthetic chemical</td>
<td>protein kinases</td>
<td>(Taylor et al. 2013)</td>
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<td></td>
<td>Diethyllobamazine (DEC)</td>
<td>synthetic chemical</td>
<td>eggs</td>
<td>(Taylor et al. 2013)</td>
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<tr>
<td></td>
<td>Flavopiridol</td>
<td>synthetic chemical</td>
<td>protein kinases</td>
<td>(Taylor et al. 2013)</td>
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<tr>
<td></td>
<td>Invermectin</td>
<td>synthetic chemical</td>
<td>eggs</td>
<td>(Taylor et al. 2013)</td>
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<td></td>
<td>Levamisole</td>
<td>synthetic chemical</td>
<td>subtype of nicotinic acetylcholine receptor (nAChR)</td>
<td>(Kaminsky et al. 2008)</td>
</tr>
<tr>
<td></td>
<td>Neomycin</td>
<td>synthetic chemical</td>
<td>protein kinases</td>
<td>(Taylor et al. 2013)</td>
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<td>Vaccine</td>
<td><em>Dictyocaulus spp.</em></td>
<td>x-irradiated L3</td>
<td>L3-stage adults</td>
<td>(Hotez et al. 2010)</td>
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<td></td>
<td><em>Echinococcus granulosus</em></td>
<td>recombinant proteins</td>
<td>EG95</td>
<td>(Hotez et al. 2010)</td>
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<td></td>
<td><em>Fasciola hepatica</em></td>
<td>cathepsin L</td>
<td>egg production and viability</td>
<td>(Sabatelli 2010)</td>
</tr>
<tr>
<td></td>
<td><em>Fasciola hepatica</em></td>
<td>anti-H-gal-GP</td>
<td>digestion</td>
<td>(Sabatelli 2010)</td>
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<tr>
<td></td>
<td><em>Necator americanus</em></td>
<td>protein-2</td>
<td>unspecified</td>
<td>(Sabatelli 2010)</td>
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<td></td>
<td><em>Necator americanus</em></td>
<td>APR1</td>
<td>inhibit parasite feeding by neutralizing enzyme activity</td>
<td>(Hotez et al. 2010)</td>
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<td></td>
<td><em>Pichia pastoris</em></td>
<td>GST1</td>
<td>inhibit parasite feeding by neutralizing enzyme activity</td>
<td>(Hotez et al. 2010)</td>
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<td>Microbial</td>
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<td>larvicidal</td>
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<td><em>Arthrobotrys musiformis</em></td>
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<td><em>Bacillus circulans</em></td>
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<td></td>
<td><em>Bacillus thuringiensis</em></td>
<td>Cry5B</td>
<td>p38 mitogen-activated protein kinase; nicotinic acetylcholine receptor (nAChR) agonist</td>
<td>(Cappello et al. 2006; Hu and Aroian 2012; Urban et al. 2013)</td>
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<td>Cry21A</td>
<td>nicotinic acetylcholine receptor (nAChR) agonist</td>
<td>(Hu and Aroian 2012)</td>
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Table 2 Non-plant based anthelmintics. Current anthelmintics are synthesized from specific lead chemicals, microbial metabolites, or parasitic worms and their activity is based on one specific target.

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<th>Target</th>
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<td>Microbial</td>
<td><em>Bacillus thuringiensis</em></td>
<td>Cry14A</td>
<td>growth and development</td>
<td>(Wei et al. 2003)</td>
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<td><em>B. thuringiensis var. kurtaki</em></td>
<td>spore crystal suspension</td>
<td>larvicidal</td>
<td>(Sinott et al. 2012)</td>
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<td><em>B. thuringiensis var. israelensis</em></td>
<td>spore crystal suspension</td>
<td>larvicidal</td>
<td>(Sinott et al. 2012)</td>
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<tr>
<td></td>
<td><em>B. thuringiensis var. osvaldocruzi</em></td>
<td>spore crystal suspension</td>
<td>larvicidal</td>
<td>(Sinott et al. 2012)</td>
</tr>
<tr>
<td></td>
<td><em>Clonostachys candidabrunic</em></td>
<td>7 metabolites (Five roselipins, linoleic acid, and aurantiogliocladin)</td>
<td>diacylglycerol acyl transferase 2</td>
<td>(Ayers et al. 2010)</td>
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<tr>
<td></td>
<td><em>Duddingtonia flagrans</em></td>
<td>chlamydomospores</td>
<td>larvicidal</td>
<td>(Larsen 2000; Waghorn et al. 2003; Waller 2006)</td>
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<td><em>Monacrosporium salicenum</em></td>
<td>secondary metabolites</td>
<td>larvicidal</td>
<td>(Liu et al. 2015)</td>
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<tr>
<td></td>
<td><em>Monacrosporium thaumasium</em></td>
<td>secondary metabolites</td>
<td>larvicidal</td>
<td>(Vilela et al. 2013)</td>
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using a variety of solvents (e.g., ethanol, acetone, chloroform, methanol, water). Each solvent will cause plant cells to release different categories of metabolites based on polarity and hydrophilicity. When combined with metabolomic analysis of each fraction, this approach is a good way to identify highly active components. However, these approaches, specifically fractionation, may overlook the synergistic role of metabolites in killing parasites. If screening of fractions is performed, combining all fractions as one treatment could be a way to quickly assess any potential synergistic activity.

4. **In Vivo tests**: Plants showing anthelmintic activity *in vitro* may not show the same activity *in vivo*. While a number of studies slaughter livestock used in *in vivo* experiments, there are more humane alternatives. Fecal egg counts can be conducted weekly or monthly during a grazing experiment (Taylor et al. 2009). No livestock are harmed in the process and vets can check livestock weekly to ensure those receiving herbal/plant-based therapeutics did not contract a life-threatening parasitic infection. In addition to conducting fecal egg counts, the number of eggs and/or larvae in soil cores and on grass samples can also be performed to establish whether there are changes in the abundance of parasites where animals are grazing depending upon treatment type (e.g., synthetic anthelmintic, bioactive forages, herbal supplement, etc.) (Lopes et al. 2016).

**Implications for Agriculture and Conservation**

The potential role of plants with potential anthelmintic properties has important ramifications for agriculture and conservation. First, a greater emphasis could be placed on cultivating these plants. For example, in semi-natural ecosystems, grazing activities could center around when these plants are in flower. In more sedentary agricultural systems, these plants could be included in pasture and/or meadow seed mixes. Second, many plants used within ethnoveterinary systems are indigenous and may be under threat. Some plants traditionally given to livestock (or naturally grazed) to control parasites are considered “weeds” that are removed to achieve conservation objectives (Lans et al. 2007). For example, conservation groups often cut down willow from wet pastures and juniper from chalk grasslands in the UK. Conservation activities could promote the active use of these plants to sustain local populations.

**Future Directions**

What role should ethnobiological research play in the development of new anthelmintics? As this short perspective piece has shown, ethnobotanical and ethnozoological research has shed light on the vast array of plants which could potentially be added to pastures and feed supplements to naturally prevent and control parasitic infection. Plants could thus provide a sustainable alternative to traditional synthetic anthelmintics. However, further
interdisciplinary and rigorous research on plant-based anthelmintics is needed. We need to establish the natural availability of secondary metabolites in specific ecosystems (e.g., pastures, rangelands) and specific plants. We also need to establish whether the metabolomic composition of these plants changes over time. To prevent needless replication of research and to make this data accessible to end-users (e.g., farmers), such research should be made publicly available. Future research could concentrate on identifying species which could be used as anthelmintic fodder trees. These would provide perennial forage and may be suitable to regions experiencing high levels of aridity and/or flooding (Figure 3). For example, in the Middle East the pods of acacia trees (e.g., *Acacia nilotica*) contain saponins and proanthocyanins (Abdel-Farid et al. 2014). These trees are drought-resistant and provide a good source of forage when other grasses, forbs, and herbs have disappeared. In the UK, willow trees (*Salix* spp.) contain high levels of salicylic acid and proanthocyanidins (Agnolet et al. 2012), and cattle roaming natural pastures often actively consume the bark of the tree when ill (French 2017). Because these trees are also good for mitigating flooding, planting more of them would have both economic and environmental effects.

More research could also investigate whether aqueous solutions made from plant crude extracts could be applied to highly infected pastures to reduce parasitic load. Finally, further interdisciplinary research on parasite ecology and livestock health should record and integrate local ecological knowledge into regional programs for controlling parasite outbreaks. For example, farmers and graziers can provide information on how changes in the weather (e.g., increased flooding) and animal husbandry practices (e.g., over-stocking) may increase/decrease parasitic infection in livestock. This information could be analyzed along with environmental, climatological, and hydrological information in geographical information systems (GIS). While perhaps optimistic, further interdisciplinary research into the bioactivity of plants traditionally used to manage parasites—and incorporation of these plants into current agricultural systems—could reduce the rise of livestock anthelmintic resistance globally.

Notes

1These include: Sustainable Control of Parasites in Sheep (SCOPS) (http://www.scops.org.uk/); the Responsible Use of Medicines in Agriculture Alliance (RUMA) (http://www.ruma.org.uk/); the Antiparasitic Resistance Management Strategy (ARMS) of the FDA in the USA; and the World Health Organization Global Action Plan (GAP) on antimicrobial resistance (http://www.who.int/antimicrobial-resistance/en/).

Declarations

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References Cited


Perspectives


Numerous studies have explored the impacts of various factors on parasitism and its control. Numa et al. (2012) compared dung beetle species assemblages between protected areas and adjacent pasturelands in a Mediterranean Savanna landscape. Their findings suggest that protection can lead to a diversity of dung beetles, which in turn can impact soil health and ecosystem services.

Patz et al. (2000) highlighted the role of environmental change in the emergence of parasitic diseases. They emphasized the need for integrated approaches to address these issues.

Piluzza et al. (2014) reviewed the role of tannins in forage plants and their implications for animal husbandry and environmental sustainability. Their work underscores the importance of understanding plant chemistry in the context of livestock management.

Ridsdill-Smith (1993) investigated the effects of avermectin residues on dung beetle reproduction and survival. This study provides insights into the potential impacts of chemical residues on wildlife populations.

Sabatelli (2010) developed a nested model to study heterogeneous mixing and vaccination, offering a new perspective on anthelmintic resistance.

Semenza and Menne (2009) explored the relationship between climate change and infectious diseases in Europe. Their research underscores the need for adaptive strategies to mitigate the impacts of global warming.

Shalaby (2013) addressed the challenge of developing strategies to overcome anthelmintic resistance. His work offers valuable insights for developing sustainable approaches.

Sinott et al. (2012) demonstrated the toxicity of Bacillus spp. against Haemonchus contortus in sheep fecal cultures, highlighting the potential for bacterial therapy in managing parasitic infections.

Taylor et al. (2009) reported on the development of anthelmintic drug targets and drugs using chokepoints in nematode metabolic pathways, a promising area for future research.

Taylor and Learmount (2010) discussed the multiple resistance to anthelmintics in sheep nematodes and compared detection methods. Their findings contribute to the understanding of resistance mechanisms.

Traversa and von Samson-Himmelstjerna (2016) investigated anthelmintic resistance in sheep gastrointestinal strongyles in Europe. Their work underscores the need for continuous monitoring and adaptation in control strategies.

Vatta and Lindberg (2006) addressed the management of anthelmintic resistance in small ruminants, offering practical solutions for sustainable livestock management.


