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Review Article

Potential of Anthelmintic Herbal Drugs against Gastrointestinal Nematodes in Farm Animals: A Review

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ABSTRACT

Gastrointestinal (GI) nematode infections are one of the most prevalent and significant problems in livestock worldwide. This study aimed to review the potential of anthelmintic herbal drugs against gastrointestinal nematodes in farm animals. Anthelmintic drugs are the most common method of controlling GI nematodes since they are simple, cheap, and provide therapeutic and prophylactic protection. However, the problem has become complicated due to the emergence of resistance to anthelmintic drugs because anthelmintic drugs are used indiscriminately to treat parasitic diseases. Anthelmintic resistance in GI nematodes of ruminants is a global problem. Many domestic animals possess multi-class resistance to all classes of anthelmintics. Synthetic anthelmintics could be unsafe as they can cause side effects and toxicity. Therefore, plants are used to develop and discover novel substances acting as anthelmintics. Herbal drugs have become increasingly popular because of their fewer side effects in recent years. Consequently, the demand for herbal formulations of anthelmintic drugs is increasing. The development of instrumental analysis accelerates the preparation of phytochemical constituents and their standardization, and this field is becoming critical for research.

1. Introduction

Helminths can affect farm animals, humans, and livestock in the tropics[1]. Helminth infections in livestock are among the most prevalent diseases in developing countries. Globally, it is estimated that about 2 billion people are infected by intestinal nematodes[2]. Helminth-borne diseases can be chronic and debilitating; they cause significant morbidity and economic and social deprivation among humans and animals[3]. Treatments of gastrointestinal (GI) nematodes in domesticated animals have an economic value as the disease may cause increased mortality, decreased live weight gain, reduced wool growth and yield, decreased fertility and milk production, rejection of carcasses or organs for human consumption, depressed appetite, impaired GI functions, changes in protein, energy, and mineral metabolism, change in water balance, and predispositions to other diseases[4].

Today, anthelmintic resistance is recognized as a problem worldwide involving the leading anthelmintic families[5]. The definition of resistance varies in different publications. According to the World Association for the Advancement of Veterinary Parasitology (WAAVP), anthelmintic resistance occurs in ruminants and horses when a drug fails to reduce fecal nematode egg count by at least 95%[6].

Tropical and subtropical climates favor for many gastrointestinal nematodes (GINs), such as *Haemonchus*

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contortus (*H. contortus*), *Trichostrongylus*, *Nematodirus*, and *Strongyloides papillosus* in domestic animals [7]. Among these GINs, *H. contortus* is the most pathogenic, widely prevalent, and dangerous worm, responsible for high morbidity and mortality in sheep and goats[8]. Synthetic anthelmintic drugs are frequently used to control GINs. However, the efficacy of synthetic anthelmintics has been reduced with the development of anthelmintic resistance. Herbal drugs are becoming more popular as cost-effective and sustainable alternatives to synthetic anthelmintic treatments[9]. Researchers have examined various plants' anthelmintic properties *in vitro* and *in vivo*[10]. Thus, continuous evaluation of efficacy for available drugs and alternate methods are necessary for controlling these GINs.

Various mixtures of dried plants or plant products, including *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), are frequently used in herbal dewormers[11-13]. Therefore, this study aimed to review the potential of anthelmintic herbal drugs against gastrointestinal nematodes in farm animals.

2. Synthetic anthelmintic drugs: Limitations, side effects, and toxicity

2.1. Albendazole

When used for short-term GI helminthiasis therapy, *Albendazole* rarely causes side effects. Epigastric pain, diarrhea, nausea, vomiting, headache, and dizziness, also allergic symptoms, such as edema, rashes, and urticaria, are transient signs of *Albendazole* toxicity in animals[14]. *Albendazole* could negatively impact children's growth when they have asymptomatic trichuriasis[15]. The most frequent adverse reaction of *Albendazole* in humans is an increase in serum aminotransferase activity; occasionally, jaundice or cholestasis may be observed. According to the previous pharmacoepidemiologic analysis, most of the adverse drug reactions in humans linked to anthelmintic therapy were caused by long-term treatment of echinococcosis or cysticercosis with high-dose *Albendazole*[15].

2.2. Mebendazole

High dosage administration of *Mebendazole* in animals resulted in transient symptoms of abdominal pain, distention, and diarrhea. In human patients receiving high doses of *Mebendazole*, allergic reactions, alopecia, reversible neutropenia, agranulocytosis, and hypospermia are common side effects[16]. In this population, the reversible elevation of serum transaminases is common. Occipital seizures may occur during *Mebendazole* therapy in children[16]. *Mebendazole* is a potent teratogen and embryotoxic in laboratory animals; negative effects in pregnant rats have been reported at single oral doses as low as 10 mg/kg[17]. *Mebendazole* should not be administered to infants younger than two years old or taken by pregnant women[16].

2.3. Praziquantel

Praziquantel's side effects in animals, including stomach pain, nausea, diarrhea, are temporary and dose-related[18]. Human's side effects are fever, pruritus, urticaria, rashes, arthralgia, and myalgia and parasite burden are often related to these side effects. *Praziquantel* -induced inflammatory reactions in neurocysticercosis can result in meningism, seizures, and pleocytosis of the cerebrospinal fluid.

2.4. Ivermectin

At very high doses, *Ivermectin* results in CNS toxicity in farm animals that manifests as lethargy, ataxia, mydriasis, tremors, and eventually death [19]. Most of the time, mazzotti-like reactions to dying microfilariae develop in infected humans injected with *Ivermectin* due to hypertensives reaction to dead microfilariae. The severity and type of these reactions depend on the microfilariae's burden as well as the type of filarial infection [20].

3. Plants

Humans and animals with parasitic infections have been treated with various medicinal plants in history. However, there are numerous issues, such as effective dose, and lethal dosage duration of administration with the development of naturally occurring compounds as drugs for humans and animals[21]. Therefore, it would be essential to investigate the possibility of creating effective anthelmintic substances. In recent years, herbal products have gained the researchers' attention due to their anthelmintic effects, ability to control parasites, minimal adverse environmental effects. In addition, an increase in synthetic anthelminthic drug resistance necessitates the need to find a substitution for synthetic anthelminthic drugs[22]. Using plants with anthelmintic properties appears to have two benefits[23]. Plant products develop resistance more slowly and a mixture of components that synergize, producing an anthelminthic effect in plant products[24]. On the contrary, synthetic drugs have one molecule acting on the parasite when not in a combination formulation. In addition, plant-produced secondary metabolites act as active ingredients in pharmaceutical formulations[25]. The primary methods of preparation used in traditional medicine are infusions and aqueous decoctions. Recognition of some plants' therapeutic properties is essential to the efficacy and credibility of herbal medicines. Therefore, experimental proof is crucial to determine plant products' efficacy as anthelmintics.

3.1. Nicotiana tabacum

Known for its narcotic properties, *Nicotiana tabacum* is

commonly referred to as tobacco. Nicotine has been identified as the primary alkaloid in the plant, and it is often cited as an efficient pesticide[26]. There have been few studies on the anthelmintic effects of tobacco on gastrointestinal parasites in sheep, swine ascariasis, adult fleas (*Ctenocephalides felis*), blowfly (*Lucilia cuprina*) larvae, nematodes (*Caenorhabditis elegans*), and ticks (*Rhipicephalus sanguineus* larvae and adults, *Ixodes ricinus* nymphs), and *Ascaridia galli*[27,28]. In addition, *Nicotiana tabacum* potentially impacts *strongyle* infections, particularly in horses[29].

3.2. Allium sativum (Garlic)

Allium sativum (Garlic) is an antioxidant that inhibits lipid peroxidation, which has a hepatoprotective effect[30]. Its main constituent, allicin, is the most abundant component, representing about 70% of the overall thiosulfinate present in garlic cloves[31]. It is responsible for its flavor and aroma as well as its potential antibacterial, antiparasitic, antiviral, and anticancer properties. Moreover, one of the most crucial elements in garlic that are essential for most of its pharmacological effects is its organosulfur compounds[32]. Ajoene, diallyl trisulfide (DTS), and allyl methyl sulfide have been identified as the primary compounds in garlic that play an important role in its antifungal, antibacterial, antiprotozoal, anthelmintic, and antiviral properties[33]. In addition, garlic can positively affect cryptosporidial infection in swine[34].

3.3. Vaividang (Embelia ribes)

The family *Primulaceae* includes the herb known as *Embelia ribes*, which is a woody climber plant. It is also known as false black pepper or Vaividang. The primary chemical constituent extracted from this plant is embelin, which carries excellent medicinal value and is used to cure various ailments and diseases[35]. Vaividang is used to treat obesity, mouth ulcers, fungus infections, mouth sores, pneumonia, mental disorders, constipation, and abdominal pain [36]. In addition, the plant has historically been used to treat skin conditions, toothaches, tonsillitis, arthritis, jaundice, bloating, and gastrointestinal nematodes[37]. In addition, it possesses several therapeutic and pharmacological properties, including antibacterial, antioxidant, anti-inflammatory, wound healing, and anthelmintic properties[38].

3.4. Biophytum petersianum (Oxalidaceae)

Biophytum petersianum has been used to treat malaria, different types of pain, and dermatitis, as well as mouthwashes and laxatives[39,40,41]. In a study in Indonesia on sheep infected with *Strongyloides,* fecal egg count decreased when sheep received *Biophytum petersianum* extract[42].

3.5. Calotropis procera (Madar)

Calotropis procera, a member of the *Apocynaceae* family, is a softly wooded, perennial shrub with few stems, branches, and leaves that are concentrated near the growing tip and have antimicrobial, anthelmintic, antioxidant, antimalarial, nematocidal, anticancer, anti-inflammatory properties[43,44]. A study indicated that *Calotropis procera* leaf powder and amprolium had comparable activity against coccidiosis in chickens[46]. In addition, Calotropis Procera extract can inhibit egg hatching, larval development, and motility of the adult worms of *H. contortus*[47].

3.6. Melia azedarach

Melia azedarach (*M. Azedarach*), also known as white cedar, is indigenous to Indomalaya and Australasia and is a member of the *Meliaceae* family[48]. Plant extracts from *Trichilia claussenii* (*T. claussenii*) and *M. Azedarach* show activity against sheep gastrointestinal nematodes (95% *H. contortus* and 5% *Trichostrongylus* species)[49,50]. A study tests the ovicidal and larvicidal effects of plant extracts, which confirms the positive effects of the plant extract on sheep *H. contortus*[51].

3.7. Benincasa hispida

Ash Gourd (*Benincasa hispida*) is believed to have originated in Java, Indonesia. The fruit could be effective in treatment of some serious illnesses, such as convulsions, asthma, cough, urinary retention, and internal bleeding[52]. Additionally, it has beneficial effects on treating tapeworms[53]. Extract of leaves of *Benincasa hispida* causes paralysis, leading to the death of *H. contortus*, especially at very high concentrations of 50 mg/ml, within a short period[52].

3.8. Bridelia retusa

Extracts of *Bridelia retusa* bark exhibit anthelmintic activity on *Trichostrongylus* species in sheep[54].

3.9. Lantana camara

Lantana camara, also known as big sage, is a member of the *verbanaceae* family. *Lantana* leaf has fungicidal, insecticidal, and antimicrobial activities[55]. It has also been used traditionally in herbal medicines as anthelmintic and various illnesses, such as ulcers, leprosy, chicken pox, rabies, itching skin, and cancer[56]. A study reported the anti-onchocercal (Onchocerca volvulus) activities of *Lantana camara*[58].

3.10. Alpinia zerumbet

Alpinia zerumbet belongs to the family *zingiberaceae*, commonly called shell ginger which has bioactive properties, including antioxidant, anti-inflammatory, fungistatic, and antibacterial activities against *Escherichia coli*, *Bacillus subtilis*, *Bacillus cereus*, with proven efficacy against human immunodeficiency virus (HIV-1) and

antiparasitic activities[57,59].

4. Conclusion

In conclusion, it is of utmost importance to provide alternative drugs due to side effects and increased resistance to synthetic anthelmintic drugs. Some herbs are traditionally used as anthelmintic drugs, and some studies have indicated such effects of some herbs on parasites. In addition, due to their fewer side effects, herbal drugs have gained significant importance in medicine over the past few years. However, more studies are needed to evaluate the effect of herbal medicine on farm animal parasites and the effective dosage of herbal drugs.

Declarations

Competing interests

There is no conflict of interest.

Authors' contribution

The final manuscript draft was reviewed by all authors, who also gave their approval.

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Ethical considerations

Ethical issues (including plagiarism, consent to publish, misconduct, data fabrication and/or falsification, double publication and/or submission, and redundancy) have been checked by all the authors.

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