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Review Paper

Improved Traditional Drugs: State of knowledge for the sustainable management of gastrointestinal parasitic nematodes of small ruminants

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Abstract

This article aims to present the current state of the fight against gastrointestinal parasites in small ruminants from Improved Traditional Drugs (DTI). A host of scientific documents were consulted by means of search engines to gather the information useful for this synthesis. The failure of conventional treatments has led to the use of new methods to treat digestive pathologies due to internal parasitism in herds of sheep and goats. These include, among others, herbal medicine, homeopathy, aromatherapy, the mixed grazing system for small and large ruminants, ... All plant parts of plants can be used in the preparation of remedies. Several scientific studies show that plants are full of chemical compounds that cause anthelmintic effects on gastrointestinal parasites in small ruminants. Literature searches have revealed that studies on DTIs in the management of gastrointestinal nematodes in small ruminants are non-existent. In addition to the forms (decocted, macerated, infused, etc.) traditionally used by breeders, there are other forms that can be used to make DTIs from plant extracts. There are capsules, capsules, tablets etc. The placing on the market of DTIs requires official authorization based on the safety and reproducibility of the products. From the documents consulted, it appears that scientific research has not yet focused on the formulation of DTIs for the treatment of gastrointestinal parasitic nematodes in small ruminants. It will be useful to manufacture them to facilitate access to veterinary care and the sustainable management of animal health.

Keywords: Improved Traditional Drugs; Gastrointestinal nematodes; Small ruminants, West Africa; Central Africa.

INTRODUCTION

Globally, animal production contributes on average to more than 40% of the Gross Domestic Product of agriculture and contributes to the subsistence of the social layer of extreme poverty[1]. For some[2], livestock is of great importance through its participation in the diversification of activities, food security, capitalization of resources, social and economic integration and its indirect economic role, in particular through use of excreta in maintaining the fertility of agricultural land[3]. Small ruminant farming is receiving considerable attention from policy makers and pastoralists due to its numerical importance in livestock systems and its contribution to the economy of countries[4]. In 2018, the FAO estimated the African small ruminant herd at 438,000,000 head of goats and 384,000,000 head of sheep. The West

African sub-region had 171,000,000 head of goats and 115,000,000 head of sheep with 1,921,000 head of goats and 954,000 head of sheep in Benin in 2018[5]. In Benin, the breeding of domestic animals is the second agricultural activity behind crop production with a contribution to the Gross Domestic Product estimated at 13.44% in 2016[6]. Despite these advantages, there are a number of health constraints in sheep and goat farming systems, including internal parasitosis. Infestation caused by gastrointestinal strongyles remains a global threat negatively impacting productivity in these farms[7]. The recurrence of cases of resistance to traditional drugs[7] and the inability of populations to access these synthetic products have led to the development of new alternative or complementary ethno-pharmaceutical solutions in the fight against animal pathologies[7,12]. These new management strategies for animal diseases exclude or considerably limit the use of conventional drugs. In fact, the use of plant species with therapeutic and anthelmintic properties[7] in veterinary medicine, has seen progress for several years[10,13] due to their effectiveness and their ability to sustainably maintain the health of animals in an eco-responsible approach[13]. In traditional medicine, the fight against gastrointestinal nematodes in small ruminants is most often based on herbal preparations. But the practice of ethno-pharmacological veterinary care still does not respect the principles of ultimate preservation of animal welfare. The methods of administration of plants are sometimes poorly understood and certain plant species used have not been studied[13]. However, for 90% of African countries dependent on external laboratories and pharmaceutical products, DTIs represent an alternative for controlling health expenditure[14]. It is useful to formulate DTIs from plant species studied and shown to be effective against parasites and to provide pharmaceutical forms suitable for the route of administration. The relatively low costs associated with the effectiveness of these African Pharmacopoeia remedies, as well as the scientific advancement of herbal therapy, underpin their development into commercial dosage forms[14,16]. The challenges of valuing traditional and scientific knowledge of herbal medicines remain and are growing in view of the persistent economic difficulties, the demographic increase of populations, the mismanagement of natural resources, as well as climate change with its disadvantages on the well-being of the environment and living beings[14]. This bibliographic review aims to gather information on the current state of use of Improved Traditional Drugs in the management of gastrointestinal nematodes in small ruminants and to identify solutions in order to allow small ruminant breeders to have access to effective, accessible, available and affordable means of control to protect the animals in their herds from this pathology.

MATERIAL AND METHODS

The searches were carried out mainly through an analysis of scientific articles, theses and books collected in the months of October and November 2020. Electronic databases such as ResearchGate, PubMed and Google scholar were exploited to identify relevant studies on Improved Traditional Medicines used in the management of gastrointestinal parasites. The following key words: Improved Traditional Medicines, animal herbal medicine, management of gastrointestinal nematodes in small ruminants, pharmaceutical dosage forms were used to access the documents exploited. These expressions have been used in both French and English to optimize the sources of information. The articles selected are those published in English or in French, containing the keywords in their title, summary or full text. Articles that did not meet these criteria were excluded. We used 43 documents in this bibliographic summary.

RESULTS

1. Gastrointestinal Parasites: Perception of Breeders and Scientists on Improved Traditional Drugs

The breeders mention as the causes responsible for internal parasitism in small ruminants: soiled pastures, pond water and rivers. Anorexia, the presence of worms in the faeces and pricked hairs are frequently characteristic symptoms of this digestive disorder[4,17]. The chemoresistance of digestive nematodes to synthetic drugs[7], has led to the use of other solutions. New techniques for the management of animal diseases are of interest to breeders, which techniques are ancestral and passed down from one generation to another for Aouadj and Benyattou[18]. Breeders justify the use of new animal care approaches for different reasons[19]. On the one hand, it is the economic aspect and the ethical aspect on the other hand, which translate respectively into the desire to reduce the costs of conventional veterinary treatments and to ensure the well-being of animals by relieving the pain imposed on them by modern medicine[19]. For Jaeg[8], zootechnical practices are strongly oriented towards an agro-ecological approach, therefore respectful of nature. In fact, some breeders have opted for herbal therapy because of organic production[19] which is quite popular nowadays among consumers of meat from small ruminants[11]. Farmers decide on the practice of alternative treatment solutions depending on the health status of the animals[19]. According to Renier[20], some breeders very rarely resort to conventional antiparasitics against internal parasitism because of the ineffectiveness of these ordinary drugs. Herbal medicines allow them to get very good results. According to the work of Aouadj and Benyattou[18], goat farmers claim that herbal medicines are effective, available and easily accessible compared to synthetic medicines. To treat diseases caused by internal parasites, which are also responsible for diarrheal diseases in small ruminants, producers make extensive use of phytotherapy[4] and benefit from training in this area for better practice. Classic dewormers are required in the event of complications at the risk of losing the animals. A combination of management methods is sometimes observed, namely: herbal medicine-homeopathy-aromatherapy-classic antiparasitic[20]. The rational use of drugs obtained from plant materials will help attract goat farming and increase zootechnical performance[18]. This practice will not only reduce the negative impact of synthetic products on humans, but it is also conducive to the preservation of nature[18].

2. Alternative methods of managing gastrointestinal nematodes in small ruminants

In recent years, plants have been widely used in veterinary medicine to treat ailments[13], especially gastrointestinal strongyles of small ruminants[10,21]. Homeopathy, herbal medicine, and aromatherapy are three alternative forms of animal health management[9,19]. The proven effectiveness of herbal remedies has motivated institutions to develop Improved Traditional Medicines[22]. Ethnobotanical studies have shown that all parts of plant species (leaves, roots, stems, bark, flowers, seeds, flowering tops, ...), fresh or dried, can be used in herbal medicine[23]. The pharmacological properties of plants are dependent on the phytoconstituents (tannins, alkaloids, terpenes, flavonoids, ...) found there and playing variable therapeutic roles[23] on NGIs in small ruminants[11]. Overall, breeders prepare herbal remedies themselves and adopt variable modes of administration according to their experience, their knowledge in the field or

the training received from people trained in veterinary herbal medicine or homeopathy[4,19]. According to Hellec and Manoli[19], the dissemination of new therapeutic approaches for the sustainable management of domestic animal health follows four successive stages. These are training, on-farm trials, group work and consultations. The training consists in the description of herd management strategies favorable to the limitation of health problems, and in the proposal of alternative solutions to treat specific diseases. The trainer emphasizes the symptoms to be observed on animals: the appearance of faeces, the condition of the eyes and hooves as well as the presentation of the hairs on the subjects. With regard to the trials, the breeders back on their respective farms, proceed to the practice of the knowledge acquired during the training. They appreciate the relevance of the training and then get involved in groups to better understand and master the methods. Also, they have the possibility of calling on experts to support them in the appropriation of a new method[19].

Grazing management, targeted treatments, tannic plants and nematophagous fungi are other alternative solutions that are used for the control of NGIs in small ruminants[17]. The grazing management method, a practice frequently encountered in organic livestock farming[17], consists of mixed grazing and rotational grazing. Indeed, it is done by the simultaneous maintenance of small and large ruminants on the same route. Thus, small ruminants (sheep and goats) and cattle feed on the same meadow in a rotating manner or simultaneously, or alternatively by alternating on a pasture. They can graze one fodder plot in turn or several plots in succession. This system helps reduce fatalities from gastrointestinal parasitism[24,25]. Cattle can consume a larva infesting small ruminants and then vice versa, disrupting the development and proliferation of strongyles to clean up the pasture. Rotary grazing has the advantage of reducing contact between individuals and infesting larvae. Mixed grazing cannot be practiced between small ruminants because they share certain species of nematodes in common[25]. The effectiveness of this plot management practice excludes overgrazing and grazing during periods of rain and extreme coolness[17]. Targeted treatments consist of choosing highly parasitized animals to administer antiparasitics. Tanniferous plants are plant species with therapeutic properties linked to the nature of their secondary metabolites and above all to the richness of their organs in tannins[26]. Tannins are precursors of anthelmintic effects on gastrointestinal nematodes of small ruminants[10,27]. Nematophagous fungi are also used as alternatives to synthetic antiparasitics. These fungi, present in soils rich in humus, attack the larvae of parasitic strongyles to limit their proliferation[17].

3. Efficacy of herbal preparations on gastrointestinal nematodes of small ruminants

The use of medicinal plants for therapeutic purposes has experienced a strong re-emergence over the past twenty years in the fight against NGIs in small ruminants[10]. The effectiveness of herbal remedies depends on the harvest season of the plant, its vegetative stage, its condition, where it comes from, but above all on the chemical constituents found there[28]. The identification of the plant species intended for the manufacture of DTIs is very important in compliance with regulatory provisions, thus contributing to the quality and safety of the finished product. The use of plant extracts to manufacture Improved Traditional Medicines requires periodic interventions in the field to assess the cultivation route, good harvesting practices and ensure the absence of contaminants in the organs of plants that will be used[28]. The conditions of plant extraction, equipment and extraction solvents used are elements capable of influencing the quality of plant extracts. The therapeutic properties of these extracts are evaluated in vitro and in vivo as well as their biological manifestations. These approaches participate in the establishment of biological and therapeutic evidence on the effectiveness of the extract[28] and of the Improved Traditional Medicine to which it will result. According to authors[29], several plant species have been the subject of scientific studies in Africa. These studies have shown that plants exhibit various anthelmintic properties on gastrointestinal parasites of sheep and goats and sometimes at different levels of their life cycle[11]. Essential oils are aromatic compounds of plant organs, full of many biochemical constituents giving them antiparasitic properties[9] on gastrointestinal nematodes in small ruminants[11].

4. Safety and reproducibility of Improved Traditional Drugs

The absence of health risk associated with taking Improved Traditional Medicines in human and animal populations is permitted by a number of successive procedures. First, testing for possible impurities is necessary to ensure that DTI is exempt from contaminants and organic pollutants capable of lingering on plants[30,31]. The formulation of Improved Traditional Medicines from plants requires periodic interventions in the field to assess the cultivation route, good harvesting practices and ensure the absence of contaminants in the plant organs that will be used[28]. Second, the safety of DTIs involves performing toxicity tests on plant extracts. These tests consist of the characterization of the intrinsic toxicity of plants, the understanding of possible functional disorders and the quantification of the effect / dose. During phytochemical analyzes, special attention is given to phytoconstituents previously recognized as toxic[8], in particular cyanogenic derivatives and sometimes phenol[32]. The phytochemical screening of extracts promotes the strengthening of quality indices of DTIs at several levels: the selection of varieties of plant species and their origins and verification of the level of stability of the products; but also to have a better understanding of the therapeutic effects and to guarantee reproducibility[28].

5. Constraints on the use of DTIs

The regulation of the marketing of DTIs imposes two main constraints: the guarantee of reproducing the same product quantitatively and qualitatively over time, and the proof of its therapeutic efficacy by highlighting its mechanisms of action[22,23]. These constraints, coupled with the current regulations on veterinary drugs[23], disrupt the expansion of the market for the sale of Improved Traditional Drugs notwithstanding the encouragement of regulatory provisions on biological products[33]. The formal introduction of DTIs in veterinary medicine mainly faces the difficulties of obtaining marketing authorization[8]. This authorization requires the safety of the drug[34], the justification of the origin of the plant species used in its manufacture as well as their traditional use. Also, it requires the efficacy of the product and the absence of residues in animal products[8,23]. Directive 2001/82 / EC indicates that a product produced on the basis of plants, recognized and intended for animals must comply with the regulations on substances for pharmaceutical use in order to obtain marketing authorization[23]. Poor countries have abundant herbal remedies, but almost all do not have rules for including traditional medicines in drug regulation[14]. But the introduction on the market of any medicinal product in West Africa requires compliance with the principle of marketing authorization contained in Law No. 54-418 of April 15, 1954[34]. Products resulting from the transformation

of plants, complying with European regulation 767/2009 / EC and which influence the well-being and gastrointestinal microbes are used as additives in animal feed or drinking water[23]. Easy access to veterinary care requires the simplification of the marketing authorization procedure for DTIs, not only because of the unsuitability of the approval procedures for conventional drugs to those derived from plants[14], but also because of their nature and the remarkable recognition of their effectiveness[8].

6. Dosage forms of DTIs and modes of administration

Traditionally, herbal medicines are used in different forms, namely: decocté, powder, poultice, infused, macerated ...[4,13,23,35]. These traditional forms are generally administered orally in small ruminants[4]. Plant powders are introduced into sterile sachets for making tea bags which will be labeled and subject to quality control. Three dosage forms of MTA are frequently used. These are: tablets, capsules, and oral fluids[16,36]. There are other forms including: capsules, alcoholates, alcoholates, fluid extracts powder in sachets[15,37].

7. Description of some forms

7.1. Solid forms of DTIs

7.1.1. Capsules

According to the French pharmacopoeia, capsules are solid-consistency preparations made from a hard shell with cylindrical parts open at one end and hemispherical bottoms, which contains a quantity of commonly used drugs at one time[38]. There are two main types of capsule preparations. There are herbal powder capsules and herbal extract capsules[37]. Plant powder capsules are obtained by spraying the whole plant and subsequently undergo calibration using a sieve used to analyze the particle size in pharmacopoeia, for example[39]. Plant extract capsules come in two forms: classic extracts and modern extracts. The former are obtained by evaporating to a fluid, soft, firm or dry consistency of an extractive solution. As for modern extracts, they are obtained by nebulization. Vegetable capsules can be stored in well labeled bottles[39], which are airtight and dry. The active substances can deteriorate after a period of two years[37].

It was formulated an antiamoebic DTI based on the plant of *Euphorbia hirta* Linn in the form of capsules in Cameroon[39]. Therefore, they believe that this dosage form is of interest to more than one. In the same country, other[16] have manufactured capsules, oral hypoglycemic DTI from *Laportera ovalifolia* whose safety and therapeutic activities are established.

7.1.2. Tablets

Tablets, dosage forms consumed orally, are defined as being solid preparations containing one or more active ingredients with excipients[40]. The dry extracts or powder of plants are the basic raw materials for the preparation of the tablets. The principle consists in agglomerating by compression in the form of powder or granules, a constant volume of particles. The particles may undergo pretreatment (granulation) when they do not have the physical properties necessary to obtain satisfactory tablets. The tablets are stored in sealed containers[37,40].

Others produced from *Laportera ovalifolia* a hypoglycemic tablet[16], Improved Traditional Drugs weighing 0.340 g and composed of corn starch at 10%, lactose monohydrate at 08%, 1.5% Talc and 1.5% magnesium stearate.

7.1.3. Capsules

Also known as soft shell capsules, they are solid consistency preparations made up of a soft shell. They are packaged in a thick envelope consisting of a single part and thus have the capacity to contain substances of liquid or pasty consistency. There are various forms, namely: oblong, oval and spherical shapes. Treatment with capsules is usually done orally. These preparations can be stored away from light, heat and moisture. This avoids the partial migration of a substance from the container into the contents or vice versa which would occur due to the nature of the materials and the surfaces in contact[37]. The table I shows the advantages and disadvantages of solid forms.

Table I: Advantages and disadvantages of capsules, capsules and tablets

Pharmaceutical forms	Advantages	Disadvantages
Capsules[37,39,41,42]	Small footprint ; easy ingestion; Small amount of liquid ingested; Storage over several months; Unpleasant taste masked; Bitter or tasteless flavor masked; Hidden hardly bearable odor; Reduced risk of error ; Reduced microbial contamination; No deterioration of the product by the solvent ; Reproducible effect; Reduced dosage.	Not fractionable form; Relatively high price; Susceptibly responsible for perforations, ulcers and bleeding; Destruction of certain thermolabile principles; Sometimes unpleasant aftertaste and strong odor; Storage limited by the fragility of the powder; Incorporation of additives to improve preservation; High dosage; Maximum two years of storage; Risk of heat damage.
Tablets[37]	Resistance to handling; Good preservation of active substances; Possibility of coating to mask an unpleasant flavor; Breakable shapes; Easy and quick to use.	Need to have a source of potable water for ingestion; Possible irritation of the digestive tract.
Capsules[37]	Better bioavailability; Pleasant absorption due to the capsule shell; Reduced number of excipients; Better conversation.	Need to have more financial means; Difficulty or impossibility of splitting up a take unit; Possibility of sticking the capsules to the wall of the esophagus.

7.2. Forms of liquid DTIs

7.2.1. Fluid extracts

The extraction solvents used to obtain these products are, among others: water, ethanol and ether[43] with sometimes the addition of glycerin[37]. The fluid extracts can be packaged in various galenic presentations (ampoules, single dose sachets, or vials). It is acceptable for a light deposit, which may contain preservatives, to form on the surface of an extract if only if the changes it makes to the extract are negligible. The storage of fluid plant extracts depends on the alcohol content of the product[37].

7.2.2. Dyes

In the French pharmacopoeia, tinctures are defined as being liquid preparations obtained for the most part from dried plants. Sometimes the materials to be extracted can undergo a pre-treatment such as inactivation of enzymes, grinding or degreasing. The tinctures contain alcohol in varying degrees depending on the plants. For very soluble active ingredients or drugs with tannins, alcohol can be at 60 ° while for resins, it will be 70 °, 80 ° or 90 °. A distinction is made between simple tinctures and compound tinctures depending on whether the extraction (maceration or leaching) by alcohol is carried out on a single plant or on mixtures of plants, respectively. The tinctures can be used internally, as a suppository, or externally[37].

7.2.3. Alcohol

They come from the alcoholic maceration (75 ° to 95 °) of the fresh vegetable matter. They are preferred over alcoholates to preserve the integrity of the active ingredients. The instructions for use of alcoholic beverages are identical to those for tinctures. To make alcoholic beverages, the average maceration time is 8 to 10 days. Decoction with boiling alcohol is also possible, if necessary to stabilize the plant[37].

7.2.4. Alcoholates

They are obtained by distillation of one or more medicinal substances (fresh or dry plants), by ethanol. The plants are first macerated in alcohol in varying degrees of 60 ° to 80 °[37]. Then, a distillation is carried out on the macerated. Colorless, alcoholates contain only the volatile principles of plants. Alcoholates are used internally, as suppositories and also externally (rubs, liniments, eye drops, toothpaste)[37].

The alcoholates manufacturing process is valid for alcoholates, with the difference that a water bath distillation completes the process. Like the solid forms, the liquid forms also have advantages and disadvantages summarized in Table II.

Table II: Advantages and disadvantages of liquid forms.

Pharmaceutical forms	Advantages	Disadvantages
Fluid extracts	Easy to use; Adjustable dosage; High concentration of active ingredients; Absence of sugar and almost alcohol[37].	Susceptible odor and taste of the product; Laborious preparation; Conservation difficulties[37,39].
Tincture, Alcohol, Alcoholate	Easy to use; Easy to transport and use; Adjustable dosage; Easy to absorb from the intestine; Important active ingredients[37].	Restricted use due to alcohol; Likely toxicity; High concentration of the product[37,43].

DISCUSSION

Analysis of the bibliography on the use of herbal medicines to treat animal pathologies and those relating to gastrointestinal nematodes in small ruminants in particular, reveals the existence of multiple practices. Herbal remedies have long been used by small ruminant breeders[10] in the face of persistent parasite resistance to conventional drugs[7]. Scientific work has shown that the therapeutic properties of herbal drugs are inherent in their phytochemical composition[27]. In addition to this alternative, breeders resort to many other methods in maintaining good herd health[17]. All of the new methods would allow less painful physical and health protection for animals[19] and save more money. There are many modern forms of preparation of DTIs available. However, do they conceal both advantages and disadvantages[37] and the choice of one of them should be made according to the favors presented by the production and conservation environment in relation to the good quality of the product. For this, it is essential to comply with the regulations in force[23] to guarantee the durability of the drug.

CONCLUSION

Herbal remedies are widely used in the management of gastrointestinal nematodes in small ruminants. They are used in many ways and scientific studies have proven their therapeutic efficacy depending on the chemical composition of plant materials. No scientific work has been done on the formulation of DTIs for the treatment of NGIs in sheep and goats, let alone domestic animals. Very little work has been done on manufacturing processes for improved forms of ATMs. The present review bodes well for the manufacture of DTIs from extracts of plants of the traditional pharmacopoeia tested effective on gastrointestinal strongyles of small ruminants.

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