Research, Society and Development, v. 12, n. 4, e21512441126, 2023
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Nematophagous fungi and their influences on parasitic control in sheep

Fungos nematófagos e suas influências no controle parasitário em ovinos

Hongos nematófagos y su influencia en el control de parásitos en ovinos

Received: 03/21/2023 | Revised: 04/08/2023 | Accepted: 04/09/2023 | Published: 04/13/2023

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Abstract
Infections caused by gastrointestinal nematodes in sheep have become a recurring problem due to the difficulty of eradicating these parasites from the environment. The use of alternative methods, such as biological control, using nematophagous fungi, is a suitable tool for producers. The objective of this review is to provide information, disseminate knowledge, and clarify doubts. Nematophagous fungi are microorganisms adapted to survive in the soil of various cultures, feeding on present, infectious, or free-living larvae, which can also be harmful. In this work, the groups and genera of interest in the context of nematodes were compiled, dividing them according to the mode of action. It is important to note that, under appropriate circumstances, the functioning of the nematophagous fungi may be impaired, even in the presence of proven larvae. Despite the numerous applications for the use of these microorganisms, the work points out some aspects, such as temperature and humidity, as determining factors. The described study concludes the different types and genera of fungi, modes of action, predation, colonization, and habits, facilitating understanding. Some difficulties need to be overcome, such as climatic variations, lack of prey, and their misuse, which it is up to the interested researcher to manipulate.
Keywords: Animal production; *Duddingtonia flagrans*; Nematophagous fungi; Parasitology; Sheep; Worm.

Resumo
As infecções causadas por nematoides gastrointestinais em ovinos tornaram-se um problema recorrente devido à dificuldade de erradicar esses parasitas do ambiente. A utilização de métodos alternativos, como o controle biológico, com o uso de fungos nematófagos, apresenta-se como uma ferramenta adequada para os produtores. O objetivo desta revisão é fornecer informações, disseminar conhecimentos e esclarecer dúvidas. Os fungos nematófagos são microrganismos adaptados para sobreviver no solo de diversas culturas, alimentando-se de larvas presentes, infecciosas ou de vida livre, podendo ser também prejudiciais. Neste trabalho foram compilados os grupos e gêneros de interesse no contexto do nematoide, dividindo-os de acordo com a forma de ação. É importante ressaltar que, em circunstâncias adequadas, o funcionamento do nematófago pode ser prejudicado, mesmo na presença comprovada de larvas. Apesar das inúmeras aplicações para o uso desses microrganismos, o trabalho aponta alguns aspectos, como temperatura e umidade, como fatores determinantes. O estudo descrito conclui os diferentes tipos e gêneros de fungos, formas de ação, predação, colonização e hábitos, facilitando o entendimento. Algumas dificuldades precisam ser superadas, como variações climáticas, falta de presas e mau uso delas, que cabe ao pesquisador interessado manipulá-las.
Palavras-chave: Produção animal; *Duddingtonia flagrans*; Fungos nematófagos; Parasitologia; Ovinos; Vermes.

Resumen
Las infecciones por nematodos gastrointestinales en ovinos se han convertido en uno de los problemas más recurrentes, debido a la dificultad para erradicar los parásitos del ambiente. La utilización de métodos alternativos, como el control biológico, mediante el uso de hongos nematófagos, puede ser una herramienta adecuada para el productor. El objetivo de esta revisión es proporcionar información, difundir conocimientos y aclarar dudas sobre los hongos nematófagos. Los hongos nematófagos son microorganismos adaptados para sobrevivir en el suelo de las más diversas culturas, alimentándose de larvas presentes, infecciosas o de vida libre, y pudiendo también ser perjudiciales. En este trabajo se han recopilado los grupos y géneros de interés dentro del contexto del nematodo, dividiéndolos según la forma de acción. Cabe destacar que, en circunstancias adecuadas, el funcionamiento del nematófago puede ser perjudicado, incluso con la presencia comprobada de larvas. A pesar de las numerosas aplicaciones para el funcionamiento de estos microorganismos, el trabajo señala algunos aspectos, como la temperatura y la humedad, como factores determinantes. En el estudio descrito, se concluyen los diferentes tipos y géneros del hongo, sus formas

de acción, predación, colonización y hábitos, lo que facilita la comprensión. Algunas dificultades deben ser superadas, como: las variaciones climáticas, la falta de presas y el mal uso de estas. Es responsabilidad del investigador interesado manipularlas.
Palabras clave: *Duddingtonia flagrans*; Hongos nematófagos; Ovejas; Parasitología; Producción animal; Vermes.

1. Introduction

Sustainability has become a key factor in the ongoing growth of the sheep industry. Alternative control methods are becoming increasingly popular, such as the use of environmental factors to fight verminous parasites like those found in pastures, which are inhabited by most parasites (Mendes et al., 2020). Microorganisms, like nematophagous fungi, that can withstand varied climatic conditions are being utilized. These microorganisms are ingested by the animals and exit the gastrointestinal tract directly into the soil. Direct inoculation in some form of food has generated promising results in reducing the successive use of anthelmintics, decreasing parasite resistance (Vieira et al., 2017, Mendes et al., 2020, Amaral et al., 2021).

Although strategies to circumvent parasitic resistance and eradicate worms in sheep farming have been increasingly present in the production scenario, the biggest challenge may still be the acceptance and adoption of these methods by producers. Non-immediate gains can lead to early dropouts, often when some control method is about to take effect, requiring persistence and patience to achieve results.

It's worth noting that the information collected in this article was compiled from different electronic databases, including Google Scholar, Scopus, and Science Direct. Additionally, this is a narrative review of articles published between 2019 and 2021.

2. Methodology

The present study was based on a compilation of information from a study using nematophagous fungi as a tool to control verminosis in the soil. Here are present all the bibliographic collected to form this compilation.

2.1 Gastrointestinal nematodes of sheep

Sheep are affected by a wide variety of parasites, especially those located in the abomasal region, or even in small intestine sections. These animals can be parasitized by several genera of nematodes at the same time, causing even more complications when it comes to controlling alternatives (Marques et al., 2021).

Among the main genera of gastrointestinal nematodes parasitic sheep are *Haemonchus* spp, *Trichonstrogylus* spp, *Trichonstrogylus* spp, *Strongyloides* spp, *Nematodirus* spp, *Cooperia* spp, and *Oesophagostomum* spp. The use of anthelmintics is still common, however, other management procedures can be equally efficient, such as rotation of pastures, alternating grazing between species, and reduction of forage height, among others (Amarante, 2009, Gonçalves et al., 2019). Some authors comment on the need to adopt preventive techniques in the control of verminous, but often this idea becomes unnoticed by producers, generating resistance (Holsback et al., 2013, Cintra et al., 2020).

In the case of nematodes, the *genus Haemonchus* spp is the most problematic, in most situations. This parasite causes serious problems in most sheep farming in which it is found, combined with the factor of anthelmintic resistance (Alemán Gainza et al., 2019). Such helminths are 1 to 3 cm long in size, and sexual dimorphism is evident, because males expose "spurious hooks" with irregular hooks at both ends of the body, on the other hand, the female has a cylindrical and uniform body, with no apparent appendages (Amarante, 2014). The evolutionary cycle of *Haemonchus* spp is direct, divided into an animal parasitic phase and free life, in which larvae develop in the soil, for subsequent animal infection.

The parasitism cycle begins with the ingestion of infected larvae (L3), along with forage, and within the digestive tract, the evolution to adulthood occurs (L5). Within the gastrointestinal tract, adults continue to feed through hematophagy, a behavior that generates problems in the ruminal environment (Girão, 1998). With the release of the eggs, these remain in the feces, occurring in contact with the soil, followed by the rapid development of approximately seven days, allowing new intake (Silva et al., 2019).

Strongyloides spp consists of the smallest genus of parasitic helminth found in sheep, with females measuring between 3 and 6 mm (Amarante, 2014). Females of *Strongyloides papillosus* reproduce by osteogenesis, generating a constant reinfection cycle, with great problematization. Like the other gastrointestinal parasites, there is a cycle of infection by ingesting L3 larvae present in pastures, with ideal temperature and humidity conditions. One of the biggest obstacles involves infections in confinements, animals are constantly infected by skin penetration, characteristic of the *genus Strongyloides* spp.

The genus *Trichostrongylus* spp is present in infestations, especially *T. colubriformis*, notably for presenting considerable resistance to anthelmintics and being very present in sheep farming (Almeida et al., 2003). Exhibiting cylindrical bodies, with a length ranging from 4 to 12 cm, the main aspects that make this species characteristic, are the ability to inhabit microvilli in the small intestine, making it impossible to observe the naked eye, besides hindering the performance of systemic drugs efficiently.

The consequences of *T. colubriformis* cause loss of protein absorption in the intestine, enteritis, especially in the duodenum, and villi become deformed and flattened, reducing the absorption area. In massive infections, weight loss is due to diarrhea associated with the drop in absorbed proteins (Osório et al., 2020). Very similar to *Haemonchus* spp, *Trichostrongylus* spp eggs are eliminated in feces, reaching the soil, developing, and propagating in the middle, later becoming ready to infect hosts. With ingestion, Larvae type L3, move to the intestinal lumen, where they penetrate the villi, maturing in L4 and L5, reestablishing the evolutionary cycle.

The control of the free life phase *for Trichostrongylus* spp is like other nematodes, the proper management of pastures can reduce the development of this species. It is not uncommon for adaptations to situations or varied hosts to occur, as in the case of the genus *Cooperia* spp. The most important species in sheep production is *Cooperia oncophora*. One of the most common problems related to this parasite is infecting sheep and cattle (Monteiro, 2019).

Regarding morphological aspects and evolutionary cycle, the nematodes of the *genus Cooperia* have a filiform body, as well as a small total length, which can be from 12 to 20 mm for females, which are considerably larger than males, with these presenting a total length, ranging from 9 to 16 mm. The large size of the female is related to the male's copulating pouch, where there is synchronism and adequacy, characteristic of this species (Ueno and Gonçalves, 1998). The pathogenesis, caused by these nematodes, consists of low absorption of nutrients in intestinal villi, resulting in symptoms such as loss of appetite, atrophy, and dark diarrhea (Toro, 2014).

The grazing environment is not necessarily exclusive to the performance of infected larvae, as highlighted by Vilela et al. (2012), some characteristic genera, in *the case of Strongyloides* spp, can infect hosts by another route, in this case, intracutaneous, allowing them to reach different product segments. Parasitism is so intense that in confinements affected by massive infestations of larvae of the *genus Strongyloides* spp, some animals may die from airway obstruction to the detriment of the parasite's cycle of this genus (Vilela et al., 2012).

It is evidenced in some regions of Brazil, with emphasis on the temperate climate (Southern region, for example) that *the species Cooperia oncophora is widely* distributed, mainly due to the presence of grazing together with cattle, this feat is peculiar for the development of this genus, added to the relatively cold and dry climate, a situation in which it favors its development (Amarante et al., 2004; Candy et al., 2018).

Toro (2014)[17] characterizes that parasites *of the genus Cooperia* spp are very similar to those of the *genus Ostertagia* spp, being macroscopic observation. The main forms of differentiation are in the copulatory pouch, larger in *Cooperia* spp, as well as transverse cuticular striations, allowing the penetration of larvae in intestinal villi. As a result, the *genus Ostertagia* spp, of small size, with females measuring between 6 and 9 mm, and males from 5 to 8 mm, is one of the main causes of parasitic gastritis in ruminants (Almeida et al., 2020).

With typically reddish coloration, these nematodes have a direct evolutionary cycle, with progression like that of *Haemonchus* spp (Amarante, 2014). The eggs of this worm are eliminated in feces, which develop over an approximate period of two weeks, until the larvae become infectants of stage L3, under favorable conditions, or are ingested by the animal, along with pasture.

Like other parasitic genera, larvae of this species have a thin cuticle, but are highly resistant, involving their body structures, this factor allows resistance to various adverse environmental conditions, as well as ingestion and swallowing, until passage through the digestive tract, reaching the favoring environment (Fanke et al., 2017).

2.2 Alternative control

Verminosis in sheep is one of the main health problems in herds. Even with numerous methodologies for control (administration of anthelmintic drugs, pasture management, interspecies management, administration of natural products, and biological control) the reduction of the parasitic load still tends to be little impacted. With this, alternative control emerges as a sustainable and viable alternative.

According to Vieira et al. (1999), phytotherapy is a way to reduce the use of conventional anthelmintics and may even increase the useful life of available chemicals, since it reduces the need to use and reuse doses of antiparasitic products over time, generating, in some situations, substantial savings. A topic of great approach in this scenario involves the use of phenolic extracts, these produce a direct impact on parasitic larvae, *especially when evaluated in vitro* but require further studies and results in vivo (Sandoval et al., 2012).

As highlighted by Petry Filho et al. (2018) plant compounds for verminous control can be beneficial and practical, often plants that are easily accessible and unable to maintain undesirable residues in the production chain are used. Oliveira et al. (2010) using aqueous extracts from banana parts (*Musa* spp) demonstrated a significant larval reduction *in Haemonchus contortus in vitro*, the authors also define that the residues were classified as easy to obtain, reinforcing the previous idea.

Other forms of control showed satisfactory results, an example of a management strategy consists of alternating grazing between species, in this case, sheep together with cattle. According to Amarante (2014) the diversity of nematode species is greater when sheep share pastures with cattle, however, due to this interaction, infesting both species, those that infect cattle end up not completing their biological cycle, followed by the death of the versts. Those with higher biotic potential continue to infect the herd, requiring other forms of population control only for the most resistant species (Monteiro, 2019).

Even though it is an alternative, this situation is not always constant, in certain occurrences, some species of parasites are established in both animals present, not only continuing their biological cycle but also generating unfavorable symptoms. Studies demonstrated by Osorio et al. (2020) with alternating grazing between cattle and sheep, being these lambs from birth to weaning and after 57 days of weaning, influenced the population reduction of adult vermins, mainly *of the genera Haemonchus* spp and *Trichostrongylus* spp in post weaned lambs, however, there were no significant reductions in the populations of *Eimeria* spp and *Strongyloides* spp in lambs before weaning.

Another option is also to reduce the height of forage, it is known that the parasite's cycle of infecting larvae is directly affected by the climatic conditions involving the grazing environment, which means that with some sudden change, an impact occurs in this cycle, whether favorable or not. If a more intense solar incidence occurs, the viable temperature for development will be high, generating a series of undesirable conditions, reducing larval viability, and consequently leading the animals to ingest fewer infecting nematodes (Rocha et al., 2007).

On the other hand, Silva Roberto et al. (2018) defines that by reducing the height of forage, infecting larvae are concentrated in greater numbers in the parts of the grass base, which leads animals to ingest larger amounts of them, often aggravating the infection already present, or causing recovered individuals to again enter worrying situations. The use of small forage species can act as an alternative, creating a reduced grazing height that allows greater infiltration of direct sunlight, causing a reduction in infectious larval populations.

The nutritional status of animals is very important, often being a viable tool, even if unnoticed, being considered as an alternative control. Animals that are supplemented with adequate amounts of protein in their diet tend to present satisfactory immune responses, being able to resist and fight parasitic infections more adequately, this should be considered in the choice of forage species or made height management, since protein levels in the diet should be strengthened (Houdijk, 2012).

The population of parasites found in pastures and soil represents a highly impacting plot in the animal parasitic load, and its control is a determining factor. When larvae found in the pasture are not properly eradicated, a portion of these occurs, leading to the resourcefulness of a term known as a refugee, consisting of a group of parasites that remain active and infectious in the soil (Costa, 2011).

2.3 Nematophagous fungi

With the growing demand on the part of producers for new alternatives in the control of verminosis in sheep, sustainable alternatives have aroused interest in the various product segments. To this detriment, biological control proves very interesting in combating worms in various forms, citing the use of predatory fungi of nematode larvae, which can attack parasitic populations directly in the soil, performing an alternative control (Araújo et al., 2004, Braga et al., 2009).

There is a growing concern on the part about the harm caused by the release of veterinary products to the environment, especially in the case of anthelmintics, which eventually end up being released into the middle through excretion, possibly causing soil contamination. Anthelmintics can be defined as one of the major players in this segment, added to its indiscriminate and high use by producers, in addition to the worsening of parasitic resistance, soil contamination soon becomes a consequence (Vassilis et al., 2016).

The use of nematophagous fungi in the control of verminosis is quite sustainable because it is a clean product, it does not release contaminants or undesirable substances into the environment, allowing better permanence. Tartarine et al. (2018) define that the use of medicines and veterinary products, mainly for parasitic control, in addition to resulting in undesirable residues in meat and soil, can directly interfere with the populations of free-living organisms, in this case, nematodes, often important and performing beneficial functions, such as predators of infectious larvae.

Most nematophagous fungi present dry spores, emerging from fruiting structures, called conidiophores, essential in the aerial dispersion of conidia. Barron (1977) defines that the structure of spores is also something important in the classification of these fungi, ranging from color, shape, and resistance to the environment. Conidiophores grow vertically, perpendicular to the substrate which the isolate has developed properly, some species produce conidiophores containing only one conidium at its end, other species have multiple branches of conidia throughout the conidiophore structure. Chlamydospores can also be produced, they are thick-walled spores, differentiated from hyphae, appear in extreme stress conditions, and can give rise to hyphae, conidiophores, and conidia, in such a way that they are present in most predatory fungi, especially those of greatest use in parasitic control (Barron, 1977).

In addition to the capture of parasitic larvae, other advantages occur, due to these fungi inhabiting the soil, such as the recycling of organic material, carbon, and nitrogen, from larval degradation (Araújo et al., 2004). These microorganisms act in

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a variety of ways, usually in the form of inert chlamydospores, which under favorable conditions, mainly involving climate, humidity, and food availability (varied larvae in general), develop into mycelium. Despite appearing as a simple denomination, nematophagous fungi have a distinct variation, the main way to distinguish them, is characterized by capture and feeding habits, dividing the genera better known as predators, ovicidal, producers of metabolites, and endoparasites of larvae (Carneiro, 1992).

2.4 Predatory fungi

Predator fungi exert a "predation" and capture activity in the soil, these hyphomycetes, when they become matured under appropriate conditions, produce adhesive traps, which propagate and spread randomly through the soil, when touched by larvae, immediately occurs a bond and immobilization of them, allowing the said fungus in question to penetrate the cell wall and feed the immobilized prey. Carneiro (1992) characterizes that the formation of adhesive traps can also be divided, according to the genus of fungi, such as the way how it spread and feed specific to its denomination, being for adhesive rings, or traps: *Arthrobotrys* spp, *Duddingtonia* spp, *Dactylaria* spp and *Dactylella* spp and genera that use adhesive mycelium: *Cystophaga* spp and *Stylophaga* spp.

These variants of fungi have some limitations, several authors describe the difficulty of implantation in the environment, such as the soil itself, because several satisfactory conditions are necessary for the correct propagation and maturation of the chlamydospores (Barron, 1977, Ritzinger, 2010). Mota et al. (2003) showed that such predatory fungi require, above all, pleasant temperature conditions for their correct development, something not often present in the national territory, the best temperature ranges range from 22ºC to 33ºC. (1999) report that the limit temperature for adequate development of these fungi is concentrated at 25ºC and if this value is translucent, its progress would be compromised.

The influence of temperature can generate suppression of fungal activity, leading to low development and propagation of chlamydospores, in addition, predatory fungi are criticized and doubted due to the lack of selectivity when predicting larvae (Silva et al., 2010). Lack of preference for predation can cause, depending on the situation, only attacks on free-living species, allowing infecting larvae to remain viable in the environment for much longer (Carneiro, 1992).

Vilela et al. (2012) performed evaluations in which goats kept in confinement were fed pellets containing *mycelium of D. Flagrans* and had considerable success in reducing the numbers of OPG for groups receiving treatment. The result of this study was mainly in the way of applying the fungus to the medium, allowing its previous maturation, until it was efficiently innocuous, thus. It was possible to observe the advance and colonization of the same direction in the substrate where the confined animals were, unlike the traditional pasture, which consisted of dry straw, commonly used as a coating for confinement floors.

Viability is very important when it comes to nematophagous fungi, as well as their form of supply, to the detriment of this, the demand for such a form arose. The most effective tool is the ingestion of reproductive structures of the fungus, which support passage through the gastrointestinal tract, following to release directly into the feces of animals, consequently attacking infecting larvae directly in the soil and continuing their development cycle (Freitas Soares et al., 2018).

2.5 Ovicidal fungi

Some fungal species attack eggs, becoming a practical tool to eliminate soil populations because destroying a significant portion of them, would imply considerably reducing the population of infecting larvae present there (Carneiro, 1992). These variants of fungi act directly by parasitizing the surface of eggs, once this process is performed, penetrate the wall, and perform absorption and transport of nutrients (Araújo et al., 1995). Despite an agent in the biological control of populations of infecting nematodes, studies denote that the action of these fungi is less active than their similar predators, generally, the preference of attack occurs in soil nematodes, which infect and destroy plant structures, to the detriment of such species depositing their eggs in gelatinous structures, whose are readily vulnerable to the colonization of fungi, different from infectious genera, which eggs in the soil are not present in this type of substance (Carneiro, 1992; Freitas Soares et al., 2018).

According to Carneiro (1986; 1992), ovicidal fungi do not depend on the larval presence to perform any control action, for this reason, their action does not affect the first generations of nematodes present but does not prevent the appearance of other future generations of larvae. Another issue that should be described is that unlike the adhesive traps produced by predators, ovicidal fungi require a long and lasting colonization time until their expected effect, to the detriment, mainly, of the presence of eggs and larval cysts ready to be attacked (Kerry, 1987). The genera best known and applied in the means of production include *mainly: Paecilomysses* spp, *Verticillium* spp, and *Dactylella* spp.

Although the application in animal production is still scarce as to studies of the action of this type of fungus, its use should be done in a somewhat strategic way. According to Gomez and Rincon (2006) simply introducing such species into an environment largely infested by larvae will not be sufficient, to the detriment of the form of attack previously mentioned, which focuses on derailing nematodes of future generations, their degrowth may be slow and unfeasible, so it is necessary first a way to reduce the current infestation and later, introduce ovicide fungi to prevent reinfestations.

One form of control that tends to be promising is the use of the combination of predators (larvicides) and ovicidal, allowing diffusion of both species in an environment, and allowing the control and eradication of all parasitic forms. Tests performed by Costa (2011) demonstrated the feasibility of using such varieties of fungi, but mainly in vitro evaluations. Still, the greatest difficulty is to apply both types in the same soil environment and affect their joint action.

2.6 Endoparasite fungi

Some varieties of fungi that inhabitant soils use varied methods to feed on their prey, when it comes to predators, previously mentioned, these make use of adhesive traps, launched in a certain space, which, in terms of possible larvae, they capture and feed. Like predators, endoparasites play an important as in the eradication of larval populations in the soil, so they could also be considered predatory fungi. To the detriment of how they feed, they launch their propagative reproductive forms, in this case, the chlamydospores, which, in contact with the cell wall of the larvae, make an active penetration y development inside them, reusing the nutrients available there (Carneiro, 1992).

Barron (1977), in one of the first in-depth studies of this species of fungus, classified that they often remain inactive for a long amount of time, to the detriment of only "activating" in the direct presence of the cell wall in a potential victim, that is, in some situations, it is necessary a very large amount of nematodes in the soil, both parasites and free life, so that the proportion found there of chlamydospores is sufficiently active. The use of endoparasite nematophagous fungi, compared to predators, is still not so intense mainly in larvae infecting gastrointestinal nematodes, much of the satisfactory results still involve applications for the control of phytomatoides, active parasites of various crops (Mendes et al., 2020).

The main known genera involve *Nematoctonus* spp, *Nematoctonus* spp, and *Panegrells* spp, with the first two being used in in vitro assays, using applications at the concentration of $1.25x10^5$ chlamydospores in populations of tomato parasitic nematodes, which are insufficient to cause any type of expected reduction (Baron, 1977). The authors denote the so-called "activity window" which would be the inert period of the chlamydospores, until the activation and attack on target larvae, this major obstacle often becomes the main problem when using fungi of such category since time can be essential in the eradication of a harmful larval population. A way to affect the action of endoparasites, in an environment impregnated with larvae, would previously be to perform a natural infection in vitro, so that the fungi obtained a more advanced stage of development, later introducing such inoculars in the desired environment, this would provide a reduction to time of action of fungi, improving their results in the attack of larvae.

2.7 Predatory fungi in sheep farming

Vieira (2017) attributes that the best way to make a biological agent more efficient is to produce it and propagate it on an industrial scale. Another weight is the cost of production, especially when compared to traditional drugs established in the market, as well as the survival time of the organism in commercial formulations. While other classifications of predatory fungi lack effective studies in sheep farming, for the determinant use of larval control, predatory fungi of larvae, especially the genera *Duddingtonia* spp, *Arthrobotrys* spp, and *Monacrosporium* spp have shown satisfactory results, especially in the case of the topics discussed earlier. The potential of these genera as controllers has practical results in in vitro experiments (Araújo et al., 2004, 2006) and in vivo conditions (Torres-Acosta et al., 2012).

One of the main reasons that lead to the inclusion of these microorganisms in commercial products is their high adaptive capacities, as well as versatility, these have the practicality of being introduced to the desired medium through the incorporation into some medium (mineral salt, protein concentrate) and consequently, passage through the gastrointestinal tract of animals, without harming highly important structures (Minguetto, 2018). Studies by Gomez and Rincon et al. (2006) in Spain, with oral administration of 5×10^5 chlamydospores of *Duddingtonia flagrans* in sheep, found a clear reduction in the number of L3 in the pasture, after 10 weeks of grazing, the reduction was more evident in the eighth week. However, no significant difference was found in EPG counts and weight gain of the animals.

The *species Duddingtonia flagrans* is still considered the most promising due to the abundance of chlamydospores, ability to resist passage through the gastrointestinal tract, and efficient soil colonization, as well as being the most studied in the control of helminths of ruminants (Mota et al., 2003, Braga et al., 2009, Paraud et al., 2005). Faedo et al. (1998) reinforce that *Duddingtonia* spp consists of the most resistant genus in existence when it comes to nematophagous species, which would make it a versatile alternative. Another factor that gains prominence is the incorporation of this fungus in commercial products, which would efficiently facilitate the introduction of animal production systems.

Like other predatory fungi already described, *D. flagrans* performs predatory action through the incorporation of adhesive nets, which are characterized by a simple hyphae system. According to Braga et al. (2008), this variation produces two types of spores called conidia and chlamydospores, however, what is most observed in culture media, as well as for facilitated propagation, are the last. As reported by Buzatti et al. (2017) the chlamydospores are extremely resistant structures, mainly to the detriment of the thick cell wall, this characteristic allows superior adaptability when compared to other variations of spores and prolonged permanence in the environment, added to the passage through the animal gastrointestinal tract.

The range of use of *the fungus D. flagrans* is immense within animal species, often allowing its application in alternative scenarios, such as the mixture of mycelium in some culture mediums, affecting their development and facilitating their post-ingestion propagation. Tests conducted by Costa et al. (2011) used mycelium from various soil samples, collected in the State of Minas Gerais - MG, mixed with a liquid medium, containing potato-dextrose, consequently being transformed into pellets for ingestion. The pellets containing mycelium of *D. flagrans* were efficient in crossing the gastrointestinal tract of asinine, as well as reducing infectious larval populations.

The supply of isolates of predatory fungi is often not as simplified as it is related, acting time is varied, called the "grace period" because, at this time, specific conditions are needed for the activation and performance of nematophagous adequately (Carneiro, 1992). Studies have demonstrated the intervention of some variables in the maturation of fungi, which may become considerable problems over time (Vieira, 2017, Ferreira et al., 2016, Serra et al., 2017). Evaluations carried out by Viera (2012) determined that the supply of varied anthelmintics, along with the supply of chlamydospores *of Duddingtonia flagrans, Arthrobotrys oligospora, Paecilomysses fumosoroseus, Paecilomysses lilacinus, Paecilomyces marquandii,* and *Paecilomyces variation*, may directly interfere in soil colonization of various genera used for parasitic control.

The influence of various antiparasitic molecules generates an inactivation effect on fungal structures, preventing them from proceeding to the maturation stage. Similar problems were observed by Braga et al. (2021) in trials using various known components on the market, including ivermectin, albendazole, and thiabendazole. It is discussed that, because these reproductive components are activated mainly by chemical variations, by pressing variations in the environment, mainly derived from such antiparasitic molecules, chlamydospores, or other fungal reproductive structures, they are unable to mature, consequently generating extremely low colonization in the intended environment.

The inhibiting effects of chemotherapy can be observed with very low concentrations, studies conducted by Vieira et al. (2017) show that in small concentrations, for one of the compounds most used in the means of treatment to infectious nematodes, 0.5 μg mL^{-1} of ivermectin is sufficient to inhibit the development of several distinct genera of nematophagous fungi, used in the biological control of infecting nematodes. Although the previously treated phenomena describe in vitro inhibitions, in vivo results are not yet as reportable, perhaps, for antiparasitic to have an action detrimental to the development of fungi, these would take long periods of successive applications, not denigrating the great benefit of using these biological controllers. Several pioneering studies have already demonstrated the proven action of these genera under infectious larvae, which evidences the possibility of using such species for the most varied forms of biological control and effective hygiene of pastures (Araújo et al., 2004).

3. Results and Discussion

Infections caused by gastrointestinal nematodes in sheep have become a recurring problem due to the difficulty of eradicating these parasites from the environment. The use of alternative methods, such as biological control, with the use of nematophagous fungi, is presented as an appropriate tool for producers. The aim of this review is to provide information, disseminate knowledge, and clarify doubts. Nematophagous fungi are microorganisms adapted to survive in the soil of various crops, feeding on present, infectious, or free-living larvae, and can also be harmful. In this work, the groups and genera of interest in the nematode context were compiled, dividing them according to their mode of action. It is important to note that, under adequate circumstances, the functioning of the nematophagous fungus may be impaired, even in the presence of larvae. Despite the numerous applications for the use of these microorganisms, the study points out some aspects, such as temperature and humidity, as determining factors. The described study concludes the different types and genera of fungi, modes of action, predation, colonization, and habits, facilitating understanding. Some difficulties need to be overcome, such as climatic variations, lack of prey, and their misuse, which is up to the interested researcher to manipulate.

In summary, the use of nematophagous fungi in the biological control of gastrointestinal nematodes in sheep may be an effective strategy, but limitations and challenges associated with their use must be considered. The dissemination of knowledge and information about the use of these microorganisms can contribute to their rational and efficient use in the field, minimizing environmental impacts and promoting the sustainability of sheep production.

4. Conclusion

Biological control with nematophagous fungi is a promising option for managing infections caused by gastrointestinal nematodes in sheep. Although there are some limitations, such as the influence of environmental factors, knowledge about these microorganisms can help in implementing effective strategies for controlling these parasites. This work presented important information on the groups and genera of nematophagous fungi of interest in the context of nematodes, offering a more complete understanding of their modes of action, predation, colonization, and habits. In summary, the use of nematophagous fungi may be a viable alternative to the use of chemicals for controlling gastrointestinal nematodes in sheep.

Acknowledgments

To CAPES, for the scholarship granted. The present work was carried out with support from the Higher Education Personnel Improvement Coordination - Brazil (CAPES) - Case Number: 88887.495433/2020-00.

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