Review Article

Treatment Approaches of Ovine Fungal Diseases using Antibiotics and Ethnoveterinary Medicinal Plants

Djadouni Fatima* and Meliani Amina
Biology Department, Faculty of Natural Sciences and Life, Mascara University, Mascara, Algeria.

ABSTRACT

Sheep and goats are both small ruminants with wide distributions due to their production of milk, wool, and meat. As such, the diseases of these animals are of great economic importance to humans. Poor nutrition, poor breeding, poor hygiene, and poor management systems are the most responsible factors of these diseases that cause annually significant livestock losses affecting the economy, animal diversity, and ecological balance. These diseases are transmitted among animals in different ways and endemic especially in large and common pastures and among the causes of their spread are contact, vectors, air, water, feeds, wastes, and pollution. Environmental conditions play an important role in increasing the spread of disease, which is often found in humid and warm seasons compared to temperate zones and Saharan zones. So through this review article, we try to show the different ancient and modern methods of treating these diseases and to share them with other societies.

INTRODUCTION

Ovine and caprine animals (sheep and goats) are ruminant herbivores of a genus of mammals belonging to the large Bovidae family. These animals contribute significantly to the economy of farmers worldwide in Mediterranean as well as African, European, and Southeast Asian countries. These small ruminants are valuable assets because of their significant contribution to meat, milk, and wool production, and potential to replicate and grow rapidly.

Several fungal diseases affected sheep and goats may lead to mortality and morbidity losses, and cause great economic losses. Pythiosis, aspergillosis, and ringworm are the common diseases that affect both bovine and ovine, and have similar symptoms and treated in the same ways as described in first part of this study.

Phaeohyphomycosis

Phaeohyphomycosis is caused by the black yeast *Cladosporium cladosporioides*, class Dothideomycetes, order Capnodiales and Davidiellaceae family. This species are ubiquitous and isolated from almost any environmental source as soil, water, plant materials, and air where its spores are important in seasonal allergic disease. Infection occurs mainly through contact or skin puncture, especially through trauma involving wood. While, this species are saprobic dematiaceous fungi, rarely causes invasive disease in animals, only infrequently associated with human and animal opportunistic infections (Seyedmousavi et al., 2013; De Graham, 2013).

* C. cladosporioides* cause pulmonary and cutaneous phaeohyphomycosis. In sheep, pulmonary infection is observed with respiratory distress signs, coughing, fever, anorexia, and death. At necropsy, abnormalities were confined to the lung, abomasums, lymph nodes, kidneys, liver, and heart. Severe hemorrhages were observed in the lungs, and vasculitis with thrombosis was apparent in various organs, which is suggestive of hematogenous dissemination (Haligur et al., 2010; Frank et al., 2011).

Moreover, subcutaneous phaeohyphomycosis is characterized by papulonodules, verrucous, hyperkeratotic or ulcerated plaques, cysts, abscesses, pyogranuloma, non-healing ulcers or sinuses. However, phaeohyphomycosis is rarely seen in goats and is caused by free-living fungus *Peyronellaea glomerata*. The disease has been recorded in Central Asia but not in the United Kingdom. It forms papules and aural plaques on the ears. It appears to be self-limiting. The treatment of choice is aggressive surgical excision of local lesions and antifungal treatment includes fluconazole, itraconazole, ketoconazole, posiconazole,
terbinafine and liposomal amphotericin B (Bensch et al., 2010; Sang et al., 2011, 2012).

**Candidosis**

Candidosis is a fungal disease affecting the mucous membranes and the skin and may cause infection of any organ or system or systemic infections. The disease is distributed worldwide in a variety of animals and is most commonly caused by yeast species of the genus *Candida* especially *Candida albicans* (Odds, 1983; Refai et al., 2017a).

This yeast is a polymorphic fungus which grows in both yeast and filamentous forms and is the most commonly recorded species in sheep and goats beside others yeasts that are responsible for the mycotic mastitis and abortion diseases including *C. krusei*, *C. guilliermondii*, *C. tropicalis*, *C. lusitaniae*, *C. parapsilosis*, and *C. glabrata* (Khan et al., 2010; Hassan et al., 2012). Diseases symptoms and treatment is described in (fungal bovine diseases 3.4 and 3.7) (Brilhante et al., 2015; Maneenil et al., 2015).

**Cryptococcus**

Cryptococcus is a systemic fungal disease that may affect the respiratory tract (especially the nasal cavity), eyes, nervous system (brain) and skin in different domestic animals. It occurs worldwide and affects immunocompromised animals, goats, and sheep causing pneumonia and mastitis but not of meningitis (Stilwell and Pisara, 2014, Refai et al., 2017b).

In addition, signs in animals may include sneezing, snorting, nasal discharge, eye problems, change in behavior, depression, disorientation, seizures, and difficulties with moving around. Moreover, the disease is caused by saprophytic and opportunistic fungal pathogens *Cryptococcus neoformans* or *C. gatti* through the inhalation of basidiospores from environment, ingestion of desiccated yeast cells or more rarely, direct cutaneous inoculation (Woldemeskel et al., 2002; Stilwell and Pisara, 2014; Refai et al., 2017b).

Cryptococcus symptoms vary depending on the organ systems affected by the fungus. Often, symptoms are systemic and nonspecific, such as diminished appetite, weight loss, or lethargy. In sheep, and goats, the lesions are restricted to the respiratory system. Azole drugs including amphotericin B (with or without flucytosine), ketoconazole, fluconazole, itraconazole, and glucocorticoids are the most commonly antifungal used for treatment. In the case of subcutaneous or internal mass, surgeriy may be performed to remove it, followed by antifungal therapy (Woldemeskel et al., 2002; Lacasta et al., 2010; Chakraborty et al., 2014).

**Malasseziosis**

*Malassezia* dermatitis or otitis is a mycotic disease caused by some *Malassezia* species including *M. sloofiae*, *M. globosa*, *M. furfur*, *M. restricta*, and *M. sympodials* and in particular *M. pachydermats* that belong to the zoophilic yeast, division *Basidiomycota*. *Malassezia* spp. are lipophilic yeasts belong to normal cutaneous or mucosal microbiota of many warm-blooded vertebrates; it is normally found in low numbers in the external ear canals, in perioral areas, in perianal regions, and in moist skin folds of some animals (Guillot and Bond, 1999; Velgraki et al., 2015; Refai et al., 2017a).

*Malassezia* species are recognized as opportunistic pathogens that play a significant role in the development of different human and animal diseases such as otitis externa or seborrheic dermatitis. Malasseziosis occurs most commonly in animals with allergies endocrinopathies (hyperthyroidism, Cushing’s disease), immunosuppressive diseases and other skin diseases. Infection occurs either when hypersensitivity to the yeast develops or when there is overgrowth of the organism (Uzal et al., 2007; Gaitanis et al., 2012).

*Malassezia* dermatitis is uncommon in goats and sheep, where poor nutrition and debilitating underlying disease appear to be predisposing factors. Lesions are nonpruritic to mildly pruritic and nonpainful, and are characterized by erythema, hyperpigmentation, scale, greasiness, yellow waxy crusts, lichenification, follicular orthokeratotic hyperkeratosis, and mild lymphocytic perivascular dermatitis. Lesions are multifocal, often over the back and trunk, and typically become generalized but tend to spare the head and legs (Bond, 2010; Eguchi-Coe et al., 2011).

*Malassezia* otitis externa is common in cattle in South America. There is a ceruminous to supplicative otitis externa caused by predominantly thermotolerant *M. sympodials* in the summer and a predominantly less thermotolerant species, *M. globosa* in the winter (Duarte et al., 1999, 2003). Allows the antifungal used to treat this disease are ketoconazole, itraconazole, fluconazole, and terbinafine (Bond et al., 2010; Cafarchia et al., 2012; Arendrup et al., 2014).

**Rhodotorulosis**

The disease results from infection with the genus *Rhodotorula*. Although the yeast is recovered word-wide from a variety of sources, infection is generally only seen in the immunocompromised host. The fungi from the genus *Rhodotorula* are imperfect basidomycetous yeast belonging to the family *Cryptococaceae* (Tuon and Costa, 2008; Vazquez, 2011).
Table I. Drug for treatment of some infectious fungal diseases in sheep and goats.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Causative organism</th>
<th>Transmission</th>
<th>Geographic distribution</th>
<th>Pathogenesis</th>
<th>Drug for treatment</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumocystosis</td>
<td>Opportunistic fungal pathogen</td>
<td>Pneumocystis carinii</td>
<td>Worldwide</td>
<td>Fatal pneumonia in immunosuppressed hosts and other</td>
<td>Pentamidine isethionate</td>
<td>de Souza and Benchimol 2005</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Class Fungus (Ascomycota)</td>
<td></td>
<td>Pathogenesis</td>
<td></td>
<td>Sakakibara et al. 2013</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Family Pneumocystidaceae</td>
<td></td>
<td>Abomasal and intestinal hemorrhage coupled with immune dysfunction</td>
<td></td>
<td>Kondo et al. 2014</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Order Pneumocystidales</td>
<td></td>
<td></td>
<td></td>
<td>Wenker et al. 2002, Malčeková et al. 2010, Zhao et al. 2015</td>
</tr>
<tr>
<td>Microsporidiosis</td>
<td>Emerging opportunistic fungal</td>
<td>Enterocytozoon bieneusi and E. intestinalis</td>
<td>Worldwide</td>
<td>Infects the intestinal epithelial cells</td>
<td>Fenbendazole</td>
<td></td>
</tr>
<tr>
<td></td>
<td>pathogens</td>
<td>Class Enterocytozoon</td>
<td></td>
<td>Lesions in kidneys</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Family Enterocytozoonidae</td>
<td></td>
<td>Diarrhea</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Class Sordariomycetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Family Microascaceae</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Order Microascales</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>verrucosum, Microsporum nanum,</td>
<td></td>
<td></td>
<td>some keratinized surfaces and ringworm of the hair and nails</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Arthroderma cuniculi, Ar. curreyi,</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Acremonium kiliense, Alternaria</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>alternata, Aspergillus flavus, A.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>versicolor, Cladosporium cario-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>cinnii, Chrysosporium tropicum,</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Anamorph, Acremonium kiliense,</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Aphanoascus fulvuscens, D-biotin,</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Scopulariopsis brevicaulis,</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Paecilomyces lilacinus</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Family Pleosporaceae</td>
<td></td>
<td>Drooping ears and swollen eyes</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Order Pleosporales</td>
<td></td>
<td>Skin lesions</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table: Drug for treatment of some infectious fungal diseases in sheep and goats.
Rhodotorula rubra (R. mucilaginosa) is the species most frequently associated with mammal infection. Rhodotorula species are commonly recovered from seawater, lakes, ocean water, plants, soil, air, food, and occasionally from humans. The genus Rhodotorula includes eight species, of which R. mucilaginosa, R. glutinis, and R. minuta were reported to cause mastitis in ruminants (Vazquez, 2011; Wirth and Goldani, 2012).

Among the few references about the pathogenicity of Rhodotorula spp. in animals, there are several reports of an outbreak of skin infections in chickens and a report of a lung infection in sheep, both caused by R. mucilaginosa. Amphotericin B, fluconazole, itraconazole, ketoconazole, posaconazole, voriconazole, and flucytosine are the main antifungal drugs for treatment of animals (Wirth and Goldani, 2012; Dhama et al., 2013). For the microorganism demonstrated resistance or reduced susceptibility to the other antifungal drugs evaluated, but only the terbinafine was active against this fungus and amphotericin B, azoles, echinocandins, and terbinafine; no effective treatment for the disease, but in 2013 a group of antifungal drugs was described from sheep including posaconazole, voriconazole, and flucytosine as well as terbinafine. These fungal infections are very important, since they mainly as subcutaneous infections (granulomatous and necrotic) or rhinofacial, nasopharyngeal, or oral infections. In animals, conidiobolomycosis caused by Conidiobolus coronatus, C. incongruus, and C. lamprauges. Conidiobolus spp. are found mainly in soil, decaying vegetation, and insects of tropical and subtropical regions, in areas of high humidity, particularly in Central America, equatorial Africa, and India; however, cases have been reported worldwide including Brazil (Silva, 2007; Aguar et al., 2014; Weiblen et al., 2016).

In animals, conidiobolomycosis caused by C. coronatus, C. lamprauges, and C. incongruus are reported mainly as subcutaneous infections (granulomatous and necrotic) or rhinofacial, nasopharyngeal, or oral infections. These fungal infections are very important, since they compromise the health status of the sheep flock and cause serious economic losses to the sheep industry (Ubiali et al., 2013; El-Shabrawi et al., 2014). However, there was no effective treatment for the disease, but in 2013 a group of antifungal drugs was described from sheep including amphotericin B, azoles, echinocandins, and terbinafine; but only the terbinafine was active against this fungus and the microorganism demonstrated resistance or reduced susceptibility to the other antifungal drugs evaluated (Tondolo et al., 2013, El-Shabrawi et al., 2014).

Other Treatments and Preventive Methods

**Apple cider vinegar, honey and salt**

Shepherds have used apple cider vinegar, honey and salt since ancient times for their great benefit in treating wounds, ulcers, fungal and bacterial infections. In addition to its effective role to (1) improves the quality and yield of wool, (2) reduces the incidence of urinary calculi and kidney stones, (3) has powerful healing, (4) cleansing, natural antibiotic and antiseptic qualities. helps with the internal and external prevention and management of itch, flea, ticks and bot flies, (5) skin conditions, arthritis, mastitis and cystitis. For treatment, apple cider vinegar is diluted and added to ovisines drinking water or used topically on sores, wounds and pimples areas, and the same method applies to honey and salt (topical) (Schmida et al., 2012; Koushleb et al., 2020).

**Garlic and onion**

They are used as a treatment to expel worms from the stomach and intestines. Protecting livestock from blood poisoning, intestinal poisoning, and various fungal and bacterial infections. Both onions and garlic work as (1) a powerful antibiotic to treat respiratory diseases such as lung infections and severe coughing. Sheep get rid of harmful bacteria and germs, (2) a strong antiseptic for the digestive system, to get rid of worms in the stomach, and a stomach cleaner, (3) boost immunity, (4) it prevents the shedding of the sheep’s fur and increases its durability and finally (5) treatment of smallpox, plague and pomegranate peel. The mashed garlic or onion were added to livestock...
water or feeds for treatment diseases or applied directly on sores, wounds and pimples areas (Schmida et al., 2012; Koushlesh et al., 2020).

**Pomegranate peel**

Adding pomegranate peel to ovine’s feed improves the quality and quantity of milk produced by them and accelerates the healing of wounds, but also cleans them of pathogens by applied the mashed peels topically on infected skin. In addition, it strengthens the immune system and helps fight diseases that affect the digestive system by adding it to the livestock feeds and water. Pomegranate peel prevents hardening of the arteries of ovines, as the peel of the pomegranate contains many antioxidants that are beneficial for their health (Schmida et al., 2012; Koushlesh et al., 2020).

**Table II. Health benefits of some medicinal plants to treat diseases in sheep and goats (Halimi et al., 1997).**

<table>
<thead>
<tr>
<th>Plant botanical name</th>
<th>Family</th>
<th>Parts used</th>
<th>Method of use (administration)</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Origanum vulgare</em></td>
<td>Lamiaceae</td>
<td>Whole plant</td>
<td>Topical Oral with feeds and water or added to treatment bath</td>
<td>Sore and pimples Stomach wounds Scabies disease Mycoses</td>
</tr>
<tr>
<td><em>Juniperus phoenicea</em></td>
<td>Cupressaceae</td>
<td>Whole plant</td>
<td>Oral</td>
<td>Wounds and sores Pneumocystosis Digestive disorders Urinary tract infection</td>
</tr>
<tr>
<td><em>Artemisia herba-alba</em></td>
<td>Asteraceae</td>
<td>Whole plant</td>
<td>Oral Topical (the leaves were burned and the ashes mixed with olive oil and applied to wounds and sores)</td>
<td>Digestive disorders Urinary tract infection Antipyretic Kill and expel intestinal worms Pneumocystosis Mycoses</td>
</tr>
<tr>
<td><em>Lavandula stoechas</em></td>
<td>Lamiaceae</td>
<td>Leaves and flowers Oral</td>
<td>Pneumocystosis Digestive disorders Urinary tract infection Mycoses Candidiasis Wounds, ulcers and infections</td>
<td></td>
</tr>
<tr>
<td><em>Peganum Harmala</em></td>
<td>Zygophyl-laceae</td>
<td>Seeds, twigs and leaves Oral or It is placed in the form of tied bundles and then soaked in water and presented to the animal</td>
<td>Kill and expel worms from stomach Mycoses Eliminate lice, parasites and insects from animal hair, wool and leather Reduce the temperature at infection</td>
<td></td>
</tr>
<tr>
<td><em>Ruta graveolens</em></td>
<td>Rutaceae</td>
<td>Whole plant</td>
<td>Oral or it is placed in the form of tied bundles and then soaked in water and presented to the animal</td>
<td>Kill and expel worms from stomach Digestive disorders Urinary tract infection Mycoses Candidiasis Wounds, ulcers and infections Pneumocystosis</td>
</tr>
<tr>
<td><em>Urtica dioica</em></td>
<td>Urticaceae</td>
<td>Leaves, seeds, veins Oral</td>
<td>Pneumocystosis Digestive disorders Urinary tract infection Mycoses Candidiasis Wounds, ulcers and infections</td>
<td></td>
</tr>
<tr>
<td><em>Malva parviflora</em></td>
<td>Malvaceae</td>
<td>Whole plant</td>
<td>Oral Topical</td>
<td>Wounds Mycoses Bites and bruises Swellings and infections Pneumocystosis Digestive disorders Urinary tract</td>
</tr>
</tbody>
</table>
CONCLUSIONS

Biosecurity and hygiene, veterinary surveillance, health and welfare programmes, buying, registering and moving sheep and goats, appropriate grazing systems and animal selection to improve resistance are the alternative management strategies to prevent and control disease in small ruminants. Also, the knowledge of medicinal herbs and their therapeutic benefit sings us away from the use of expensive antibiotics and their side effects on animal health and nature.

Statement of conflict of interest

The authors have declared no conflict of interest.

REFERENCES


Treatment Approaches of Ovine Fungal Diseases


