

Review

Current Challenges for Fasciolicide Treatment in Ruminant Livestock

José Antonio Castro-Hermida,¹ Marta González-Warleta,¹ Victoria Martínez-Sernández,^{2,3} Florencio M. Ubeira,^{2,3} and Mercedes Mezo^{1,*}

Pharmacological treatment remains essential to control fasciolosis in areas where infection is endemic. However, there are major constraints to treating food-producing animals. Of particular concern is the lack of flukicides for treating early *Fasciola* infections in ruminant livestock in some countries. In addition, the information provided in package leaflets, particularly regarding withdrawal periods, is often incomplete, confusing, and/or contradictory. International regulatory bodies should harmonize the use of flukicides in livestock in favor of fairer, safer international trade. In addition, monitoring the efficacy of fasciolicides on farms is also essential to minimize the spread of drug-resistant populations of *Fasciola*. The current situation regarding flukicide formulations in the European Union and other, non-European countries is analyzed in this review paper.

Pharmacological Treatment Is Still Essential to Control Fasciolosis in Livestock

Fasciolosis (see [Glossary](#)) is a severe parasitic disease that causes major economic losses in pasture-fed ruminant production systems [1–5]. It is also a **zoonosis** recognized as a major public health problem in some countries [6]. In the absence of a commercial vaccine [7], strategies for reducing the impact of fasciolosis rely on the following: (i) the use of sensitive and specific methods to diagnose *Fasciola* infections in both the definitive [8–12] and intermediate [13–15] **hosts**, and subsequent pharmacological treatment of the infected ruminant livestock, which are **reservoirs** of the disease; and (ii) prevention of infection of livestock, during grazing, by reducing snail populations via drainage or enclosure of flooded grassland areas [16]. Proposals for integrated control of fasciolosis have been accurately and comprehensively addressed in recent reviews [16,17]. However, these strategies are not feasible for most farmers, and diagnosis and pharmacological treatment therefore continues to be the main option used to preserve livestock welfare and productivity [18,19], as well as to reduce the risk of human infections. Unfortunately, pharmacological control of fasciolosis is challenging due to the small number of **active substances** available (mainly for treating the earliest stages of infection), the appearance of drug-resistant flukes ([Box 1](#)), and the need to respect the **withdrawal periods (WPs)** established for treating livestock. In this context, and given the increasing consumer concern about food safety, we reviewed the status of therapeutic control of fasciolosis, focusing on the design of efficacy studies, conditions for use of available **flukicide** formulations, and restrictions or recommendations established by different regulatory bodies. Our aim is to raise awareness among veterinarians, pharmaceutical companies, and regulatory bodies about the rational use of flukicides around the world in order to minimize both the emergence of resistance and exposure of consumers to the drug residues.

Efficacy of Flukicidal Drugs

At present, there are seven commercially available compounds with reported therapeutic activity against *Fasciola* [20–22]. According to chemical classification ([Box 2](#)), these compounds include two benzimidazoles (albendazole and triclabendazole), one halogenated phenol (nitroxylnil), three salicylanilides (closantel, oxclozanide, and radoxanide) and one sulphonamide (clorsulon). As well as

Highlights

Chemotherapy remains the main tool for controlling fasciolosis in endemic areas. However, treatment of ruminant livestock, the main reservoir of the disease, faces severe technical and legal challenges.

The scarce number of flukicide drugs is particularly challenging for some productive sectors.

Therapeutic failures have been reported for all available flukicides, but the causes have rarely been identified. This situation is a matter of concern and should be considered a research priority.

The information provided in package leaflets about the conditions of use of flukicides is not always as detailed and accurate as it should be. Moreover, the efficacy of treatments is not usually monitored.

There are unexplained significant differences between countries, and even within some countries, regarding the withdrawal periods established for veterinary medicines with very similar pharmaceutical formulations.

¹Laboratory of Parasitology, Centro de Investigaciones Agrarias de Mabegondo, AGACAL, Abegondo, A Coruña, Spain

²Department of Microbiology and Parasitology, Faculty of Pharmacy, University of Santiago de Compostela, Santiago de Compostela, Spain

³Institute of Research on Chemical and Biological Analysis (IACBUS), University of Santiago de Compostela, Santiago de Compostela, Spain

*Correspondence: mercedes.mezo.menendez@xunta.es (M. Mezo).