The Environmental Impact of Medicated Grit

A Review

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Contents

Suggested Reference: Meister, F. J., Williamson, L., and Hesford, N. (2025) The Environmental Impact of Medicated Grit.

Executive Summary

In February 2025, the British Association for Shooting and Conservation (BASC) issued an invitation to tender for an ' assessment of the use and impacts of medicated grit for red grouse – Lagopus lagopus scotica.' The deliverables of the project were defined as follows:

- A comprehensive review of the use of flubendazole in red grouse, historic trends in use and when and where it is used.
- A comprehensive review of the impacts of medicated grit on red grouse and the broader upland ecosystem including flora, fauna, and contamination of soil and water.
- An overview of suggested improvements to practitioner guidance and an explanation of alternative options to the use of flubendazole.
- A synthesis of knowledge gaps, recommendations for future research and suggested alternative methods of controlling the levels of strongyle worm.

The Game and Wildlife Conservation Trust (GWCT) Scotland secured the tender with a proposal for a Rapid Evidence Assessment on 'the impacts of medicated grit on red grouse and wider upland biodiversity including evidence on the potential for contamination of water and soils.' Following the formation of the steering group in April 2025, the research question was defined as 'What are the ecological impacts of medicated grit in the uplands?'

An initial database search was designed so as to capture only studies relevant to the use of medicated grit as part of grouse-moor management in the uplands of the United Kingdom (UK). As this search returned no relevant results, we decided to extend the search to the environmental impacts of fenbendazole and flubendazole in general, in the hope that effects observed elsewhere might be applicable to UK uplands as well.

The database search and subsequent relevance screening retrieved twenty-five relevant studies. Overall, studies reported no or little toxic effect of the two anthelmintics on terrestrial environments. However, toxic effects were reported for aquatic environments, especially fish and invertebrates. Reducing the risk of contaminating water features emerges as a key objective of sustainable grouse-moor management. Reviewing the available best-practice guidance, we conclude that this risk is effectively minimised where this guidance is adhered to.

This review also identified a substantial number of knowledge gaps regarding the environmental impact of medicated grit in UK uplands and makes three suggestions for future research:

1. A field study measuring concentrations of flubendazole in water samples derived from grouse moors.
2. A laboratory study measuring concentrations of flubendazole and metabolites in the faeces of red grouse.
3. A laboratory study analysing the biotransformation of flubendazole in key moorland vegetation.

Introduction

Endemic to the United Kingdom (UK), red grouse (*Lagopus scotica*) (taxonomy as per Gill et al. 2025) is a culturally and economically important game species (Werritty 2019). Moorland managed for recreational hunting of red grouse ('grouse moors'), provides biodiversity and ecosystem services and supports unique, rare and, in some cases, internationally important plant and animal communities (Thompson et al. 1995, Newey et al. 2016, Mustin et al. 2018). Grouse-moor management includes the management of habitats, predators, and diseases to benefit red grouse and to sustain the densities of birds needed to support grouse shooting.

Red grouse in the UK, in common with many other grouse species throughout the Western Palearctic, show multi-annual population fluctuations. Hudson (1986) demonstrated that in managed populations of red grouse, these fluctuations are at least partly caused by the intestinal parasitic nematode *Trichostrongylus tenuis*. This led to early field trials of administering a broad-spectrum anthelmintic, fenbendazole, via quartz grit coated in a kernel fat (Hudson and Dobson 1989, Hudson 1992).

Fenbendazole is part of the benzimidazole family of anthelmintics, which selectively bind to the ß-tubulin protein of parasites and prevent the formation of microtubules, an essential component of the cytoskeleton, thereby causing the death of the parasite (Lacey, 1990). Commercialised as Panacur (Intervet International B.V.), fenbendazole is widely used to treat gastrointestinal parasites of livestock, poultry and domestic pets, and is usually delivered orally through boluses, medicated feed, or medicated drinking water (Lewis et al 2016). The practice of using medicated grit containing fenbendazole to treat *T. tenuis* infections in red grouse has been in place since the late 1980s, alongside other management practices, to maintain the densities of birds needed to sustain driven grouse shooting (Hudson 1992, Newborn & Foster 2002).

A revision of medicated grit in 2007 led to a change of the active ingredient from fenbendazole to flubendazole, commercialised as Flubenvet (Elanco GmbH / Kernfarm B.V.). Like fenbendazole, flubendazole is part of the benzimidazole family of anthelmintics and has a similar mode of action and delivery (Nixon et al. 2020). However, flubendazole is a compound more widely licensed for use with game bird species (GWCT 2020). In addition to altering the active component, the 2007 revision also changed the binding fat to a stearate coating, which was more temperature resistant, improving the persistence of the medicated coating in warmer weather (Baines et al. 2019). The increased persistence of the compound, however, necessitated the introduction of a minimum withdrawal period from the environment twenty-eight days before the opening of the red grouse season (12 August to 10 December) under the Veterinary Medications Regulations 2013.

Since its introduction, the use of medicated grit has increased substantially, and the majority of grouse moors now likely use medicated grit as part of their game bird management. The widespread use of medicated grit and associated greater grouse densities may, however, have caused other problems including the emergence of other density-related diseases, such as respiratory cryptosporidiosis (Baines et al. 2020). Another area of concern was the greater likelihood of flubendazole resistance in *T. tenius* (Baines et al. 2019, Cox et al. 2010). Gastrointestinal nematode resistance to benzimidazole-class anthelmintics is already reported in sheep, cattle, and horses in the UK, reducing the efficacy of these medicines and with the potential to adversely affect animal welfare and livestock productivity (BVA 2025). Concerns that indiscriminate and prophylactic prescription of medicated grit for red grouse may lead to resistance have similarly been raised (Baines et al. 2019), although this has not yet been detected (Webster et al. 2008, Cox et al. 2010).

In addition, a report submitted to the Scottish Government by the Grouse Moor Management Review Group raised concerns about the potential effect of flubendazole on the environment through unintentional run-off (Werritty 2019). However, as acknowledged in the report, there are substantial knowledge gaps on the potential environmental and biodiversity effects of medicated grit. A review of the use and impacts of medicated grit for red grouse is therefore needed and timely. Here we present the findings of a Rapid Evidence Assessment on the biodiversity impacts of medicated grit.

Methodology

Overview

A Rapid Evidence Assessment (REA) (sensu Collins et al. 2015) of peer-reviewed literature was undertaken to assess the ecological impacts of the use of medicated grit in UK uplands. REAs provide for a more transparent and quantitative review of literature than traditional literature reviews and are less time-consuming and expensive than a full Systematic Review or Meta-Analysis. While the REA approach is intended to provide as balanced, systematic, and thorough a review as possible, it should be noted that the results will not be as robust as a full systematic review.

Database search

A database search was designed to produce a literature review that would be reproducible and to minimise bias as far as possible. Web of Science and Scopus were chosen as databases for the literature searches, as they index most relevant scientific literature and facilitate reproducible searches via precisely defined Boolean search strings. The absence of these features in Google Scholar led to the exclusion of this search engine from this review.

The search strings developed aimed to retrieve as many relevant studies as possible. To this end, search strings were kept broad. Database searches were conducted in May 2025 using the following search strings:

Table 1. Search strings for database searches

	Web of Science	Scopus
Search String	TS=("flubendazole" OR"fenbendazole	TITLE-ABS-KEY ("flubendazole" OR "fenbendazole")
Papers Retrieved	2,355	4,052

Retrieved references were managed through Mendeley Reference Manager. 1,323 duplicates were removed, leaving a total of 5,084 references for relevance screening.

Relevance screening

Relevance screening was designed to ensure that each reference included in the review was concerned with the ecological impacts of the use of medicated grit (fenbendazole or flubendazole). The following inclusion criteria were applied:

1. *The study must be an original empirical investigation. Studies exclusively based on the results of other studies, for example systematic reviews or meta-analyses, were excluded as they create risk of double counting results.*
2. *The study must investigate unintended effects of fenbendazole and/or flubendazole on non-target species. Studies solely investigating the intended effect of the anthelminthics on target species (Trichostrongylus tenuis), or within or without the medicated host, were excluded.*
3. *The study must report an effect of fenbendazole and/or flubendazole on a discrete species or group of species. Studies merely reporting on concentrations of either anthelminthic in terrestrial or aquatic environments, without an assessment of the impacts on these environments and associated species groups, were excluded.*

Additional literature sources

Following relevance screening, the short list of included studies was circulated internally within the GWCT to ensure that no relevant grey literature had been missed from the database search. Additionally, the bibliographies of included studies and of meta-analysis and systematic review studies excluded under criterion 1, were searched by one of two researchers (FM/LW) to identify any additional relevant studies.

Quality assessment

Quality assessment was undertaken to allow efficient and objective evaluation of relevant references. Following a trial of comprehensive questionnaires with graded assessments, as recommended for instance for REAs (Collins et al. 2015) or evidence reviews (Stone 2013), and after consultation with BASC, these were deemed too detailed to meet this requirement. Instead, a simpler model was developed where references were subjected to a series of binary questions to objectively and efficiently assess study design robustness. Two separate sets of questions were employed, one for empirical studies and one for predictive modelling studies.

Empirical studies

1. *Is the study experimental rather than correlative?*
2. *Is there temporal replication?*
3. *Is there spatial replication?*
4. *Is the design informed by a Power Analysis or appropriate alternative approach to minimise effect-size assumptions?*

5. *Are the results presented with an indication of precision (e.g., variance, standard error, confidence intervals)?*

Predictive modelling studies

1. *Are model assumptions stated explicitly?*
2. *Is there a validation?*
3. *Is there a sensitivity analysis?*
4. *Is there a justification for resolution and scale?*
5. *Are the results presented with an indication of precision (e.g., variance, standard error, confidence intervals)?*

The number of affirmative answers returned by a given study provided its quality score, with a potential maximum score of five, which was expressed in the citation as a number of asterisks (e.g., Bundschuh et al. 2016***). It should be emphasised that the simplified quality score deployed was not an absolute metric of scientific robustness, but an indicator of the presence or absence of certain features considered important in the present context. Each relevant study was quality-assessed by one of two independent researchers (FM/LW). In instances where there was uncertainty whether a criterion had been met for a particular study, the second researcher reviewed the paper and results were discussed until a final score was corroborated.

Characteristics of Included Studies

Following relevance screening, twenty-four studies met inclusion criteria while one additional, relevant study (Chen et al. 2021) was identified through the bibliography of an included study. A total of twenty-five studies were therefore submitted for quality assessment (Table 2). Of these, twenty-three were empirical studies while only two were considered to be predictive modelling studies. Of the relevant papers, two were considered high-quality (****), eleven moderate-quality (***), and twelve low-quality (* or **).

Table 2. Characteristics and distribution of quality assessment scores of studies meeting inclusion criteria

Study Type	Reference	Q1	Q2	Q3	Q4	Q5
Empirical	Bundschuh et al. 2016	X		X		X
	Carlsson et al. 2013	X	X			X
	Carlsson et al. 2018	X				X
	Chen et al. 2021			X		
	Goodenough et al. 2019	X			X	X
	Grønvold et al. 2004	X		X		X
	Kim et al. 2010	X		X		X
	Kim et al. 2023	X		X		X
	Kumirska et al. 2016		X	X		
	Oh et al. 2006	X				X
	Park et al. 2009	X		X		X
	Podlipná et al. 2013	X		X		
	Puckowski et al. 2017	X		X		X
	Raisová Stuchlíková et al. 2018	X				X
	Sommer and Bibby 2002	X		X		
	Strong et al. 1996	X		X		X
	Stuchlíková et al. 2016	X				X
	Svendsen et al. 2002	X	X	X		X
	Svendsen et al. 2003	X	X	X		X
	Svendsen et al. 2005	X	X			X
	Teglia et al. 2025			X		X
	Van der Steene et al. 2010	X	X	X		
	Wagil et al. 2015	X		X		
Modelling	Boxall et al. 2007	X				
	Kim et al. 2008	X				

The low frequency of predictive modelling studies fulfilling the inclusion criteria prevents analysis of the quality characteristics of this type of study. With regards to empirical studies, the absence of a Power Analysis was very prominent, as Question 4 was only reported as present for one study (4%). From the information provided by the remaining studies, it was not possible to determine whether these studies failed to conduct a Power Analysis or whether this was not reported in the final publications. Additionally, relatively few studies demonstrated temporal replication in experimental design, with only six (26%) empirical studies scoring affirmatively for Question 2. The question returning the most affirmative answers was Question 1 regarding whether the study was experimental rather than correlative, with 97% of empirical studies scoring affirmatively. No study scored affirmative answers for all five questions. Conversely, no paper failed to achieve a single affirmative answer.

The geographical distribution of studies was diverse, encompassing four continents (Figure 1). 12% of studies which met inclusion criteria were conducted in the United Kingdom. The majority of studies included (n = 20) were conducted within the past 20 years, with a range of 1996 – 2025. This distribution likely reflects the increasing availability and application of fenbendazole and flubendazole as anthelmintics.

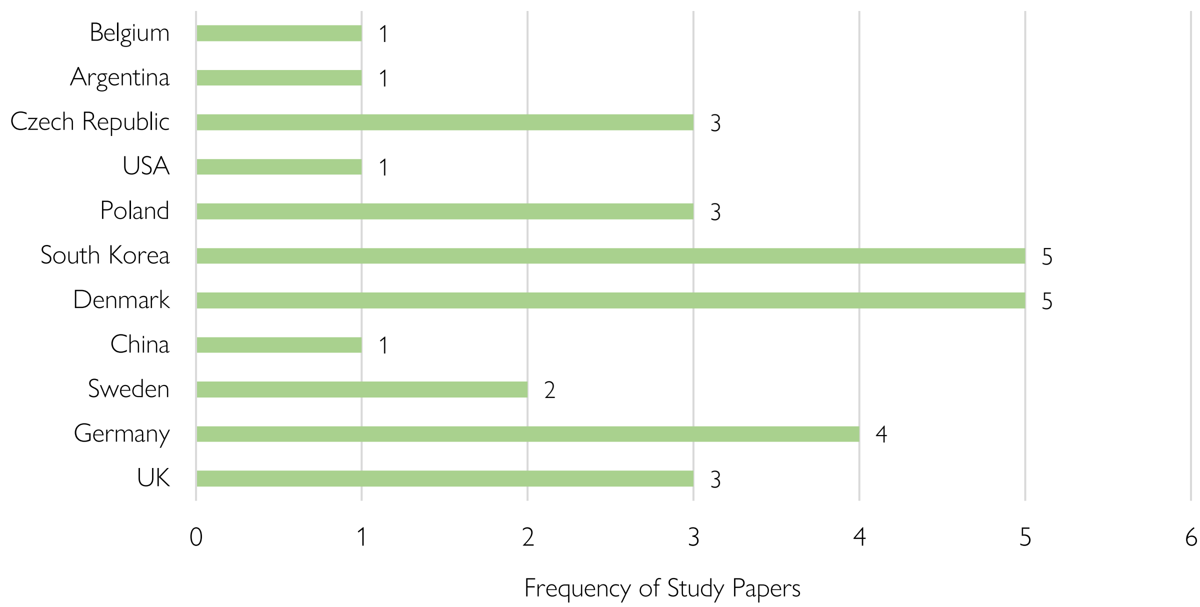

Figure 1: Geographical distribution of studies meeting inclusion criteria

Pertaining to the drug compounds of interest, the majority of studies fulfilling the inclusion criteria investigated the effects of fenbendazole (n = 13) or the effects of both fenbendazole and flubendazole (n = 9). Very few included studies investigated solely the effects of flubendazole (n = 3) (Figure 2).

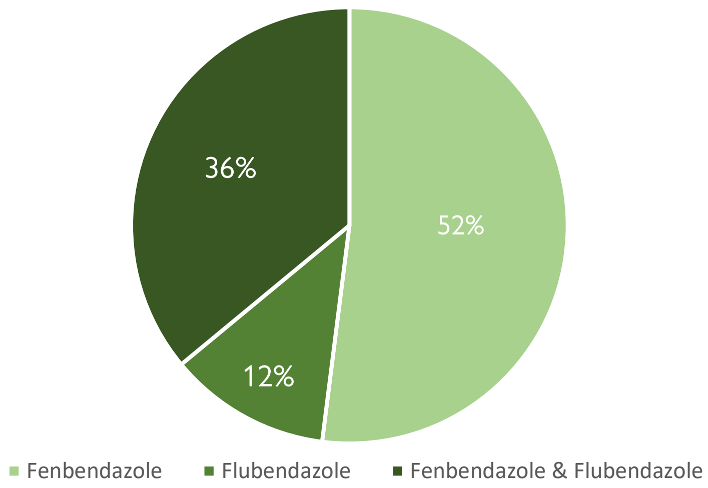

Figure 2: Drug compound of interest of interest of included studies.

There was a relatively equal distribution of studies investigating the effects of fenbendazole and/or flubendazole in aquatic (n = 13), terrestrial (n = 11) or both (n = 1) environments (Figure 3).

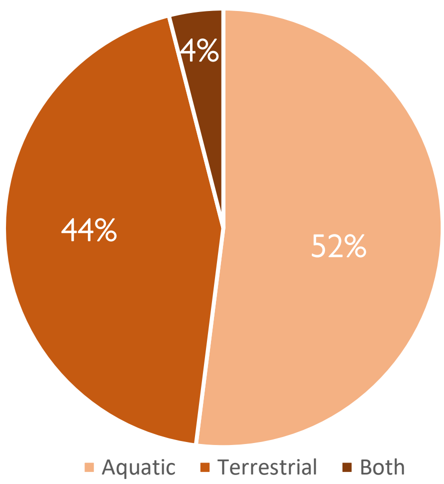

Figure 3: Broad ecological biome of interest of included studies.

Results Synthesis

Table 3: Summary results for the reported effects of fenbendazole and flubendazole on major species groups. '+' refers to a study reporting no effect, '-' to a study reporting negative effects, '±' to a study reporting mixed effects. Parentheses indicate that a study did not demonstrate an effect directly but inferred it from a related effect

		Fenbendazole	Flubendazole
Terrestrial	*Invertebrates*	+++++++ –	
	Microbes	(–)	
	Plants	++	+++
Aquatic	*Fish*	+ – – –	
	Amphibians	–	
	Invertebrates	– – – – – – – –	– – – – – –
	Microbes	++ ±	++
	Plants	+ ±	+

Terrestrial ecosystems

1. Invertebrates

Included studies researched multiple invertebrate taxa. This included annelids (earthworms), dung-colonising Coleoptera (beetles) and Diptera (flies), the larval stages of dung-beetles, specific dipteran pests, and a free-living soil nematode.

Two studies found no adverse effects of fenbendazole on the survival, growth, cocoon production, and fecundity of the common earthworm (*Lumbricus terrestris)* (Svendsen et al. 2002****; Svendsen et al. 2003****; Svendsen et al. 2005***). Svendsen et al. 2003**** also found no adverse effect of fenbendazole on the biomass of the five most abundant earthworm species (out of eleven). In contrast, one study found that fenbendazole exposure of *L. terrestris* in laboratory conditions over twelve weeks was associated with a 55% mortality rate (Goodenough et al. 2019***).

One study found no toxic effect of fenbendazole on dung-colonising Coleoptera and Diptera (Strong et al. 1996***). Another study concluded that, due to a lack of data, it was not possible to assess the effects of fenbendazole on horn fly (*Haemotobia irritans*), stable fly (*Stomoxys calcitrans*) and house fly (*Musca domsesticus*) populations (Boxall et. al. 2007*). One study reported that the number and development of dung beetle larvae (*Aphodius* spp.) in cow pats containing fenbendazole and in control pats were similar (Svendsen et al. 2003****). One study found no acute toxic effect of fenbendazole in naturally excreted concentration on the population growth of the soil nematode *Pristionchus maupasi* (Grønvold et al. 2004***).

2. Microbes

One study reported a negative effect of fenbendazole on the decomposition of dung organic matter in soils. The study inferred that this effect was caused by a negative effect on either detrivores or fungi (Sommer and Bibby 2002**).

3. Plants

Three studies analysed the biotransformation pathways of fenbendazole and/or flubendazole in plants using in vitro callus cells. Podlipná et al. 2013** reported that common reed *Phragmatis australis* took up flubendazole to a point where its metabolites could be considered inactive. Stuchlíková et al. 2016** found no acute toxicity of fenbendazole or flubendazole on harebell *Campanulla rotundiflor*. Both compounds were metabolised by harebell cells, and metabolites could be considered deactivation products. Raisová Stuchlíková et al. 2018** found that fenbendazole and flubendazole were biotransformed into their metabolites by ribwort plantain *Plantago lancelota*. These studies implied possible mechanisms for storing fenbendazole and flubendazole (and metabolites) and for limiting environmental infiltration. However, all three also caution that some metabolites remained biologically active, while other could be decomposed back to the parent anthelmintic, thus posing a potential risk to free-living invertebrates.

Aquatic ecosystems

1. Overall risk

Several studies carried out Environmental Risk Assessments of fenbendazole and/or flubendazole based on the occurrence and concentration levels detected in various aquatic environments. Kumirska et al. 2016** calculated risk quotients for fenbendazole and flubendazole in water, sediment, and fish tissue below 1, meaning no risk to the environment. Chen et al. 2021* calculated a risk quotient below 0.1 for flubendazole across 31 sampling sites, while fenbendazole was between 0.1 and 1, indicating a potential medium risk. Van de Steene et al. 2010** calculated a hazard quotient of 0.08 for flubendazole, meaning that flubendazole posed a low environmental risk. In contrast, Kim et al. 2008* determined a very high hazard classification for aquatic toxicity for fenbendazole, based on its usage and leaching potential in South Korea.

Kim et al. 2010** calculated high hydrophobicity and sorption coefficients for fenbendazole and flubendazole. Flubendazole was lower than fenbendazole but remained high overall. This indicates strong sorption of both compounds to dissolved organic components of sewage sludge. Both compounds are likely to be effectively extracted by conventional waste water treatment and bound to sludge.

2. Fish

All included studies which assessed specific fish taxa used the same model organism – *Danio rerio* (zebrafish). This is a widely used freshwater fish species in experimental and toxicological research.

One study found that fenbendazole exposure of the zebrafish induced abnormal development of the head, eyes, and tails as well as absent circulation and oedema and mortality at higher concentrations. Among fifteen veterinary pharmaceuticals tested, fenbendazole had one of the steepest concentration-response curves, indicating a small margin between concentrations resulting in no effect and high toxicity (Carlsson et al. 2013***). In contrast, Carlsson et al. 2018** concluded that fenbendazole exposure did not cause differences in swimming activity compared to the control group.

One study found that flubendazole exposure reduced survival rate, hatching rate, and heart rate, and induced pericardial oedema, yolk sac oedema, head and eye deformities, and axial malformations in a concentration-dependent manner in *D. rerio* (Kim et al. 2023***).

One study carried out an Environmental Risk Assessment for fenbendazole and found it to pose a high risk to fish in river water and wastewater (Teglia et al. 2025**).

3. Amphibians

One study carried out an Environmental Risk Assessment for fenbendazole and found it to pose a high risk to anuran species (frogs and toads) in river water and wastewater (Teglia et al. 2025**).

4. Invertebrates

A diverse range of freshwater invertebrate taxa were researched by included studies, spanning cladocerans (water fleas, represented by *Daphnia magna*), freshwater flatworms (*Dugesia gonocephala*), freshwater annelids (freshwater worms, *Tubifex tubifex*), dipteran midges and crustaceans such as the amphipod *Gammarus pulex*.

Two studies reported acute toxic effects of fenbendazole and flubendazole on *Daphnia magna*. Bundschuh et al. 2016*** reported Median Effective Concentrations (EC_{50}) (the concentration at which an effect is observed in 50% of the test population) of 16.7 µg/l for fenbendazole and 70.1

μg/l for flubendazole at 48 hours. Wagil et al. 2015** reported 19μg/l for fenbendazole and 45μg/l for flubendazole at 48 hours. Oh et al. 2006* reported 16.5 μg/l for fenbendazole and 66.5μg/l for flubendazole at 48 hours. Puckowski et al. 2017*** found that fenbendazole and flubendazole individually showed high toxicity towards *D. magna*, and that mixtures of the two compounds caused an effect in accordance with Concentration Addition-based predictions (rather than Independent Action).

One study reported particularly low EC_{50} of fenbendazole and flubendazole for *Dugesia gonocephala* (44.2 μg/l and 21.9 μg/l), *Tubifex tubifex* (32.0 μg/l and 22.1 μg/l), and *Gammarus pulex* (146.4 μg/l and 105.4 μg/l) (Bundschuh et al. 2016***). One study reported toxic effects of fenbendazole on harlequin fly (*Chironomius riparius,* freshwater midge), affecting molecular, hormonal, and developmental processes (Park et al. 2009***).

One study carried out an Environmental Risk Assessment for fenbendazole and found it to pose a high risk to crustaceans in river water and wastewater (Teglia et al. 2025**).

5. Microbes

Two studies found no acute toxic effect of fenbendazole or flubendazole on *Vibrio fischeri*, a bioluminescent bacterium. Oh et al. 2006** calculated very high Median Inhibition Concentrations (IC_{50}) (the concentration at which the bacteria's luminescence was reduced by 50%) for fenbendazole (1,570.6μg/l at 5 min, 798.4 μg/l at 15 min) and flubendazole (852.8 μg/l at 15 min), suggesting very low sensitivity to the two compounds. Wagil et al. 2015** found no effect of fenbendazole or flubendazole exposure on the luminescence of *V. Fischeri* up to the highest concentrations tested.

One study carried out an Environmental Risk Assessment for fenbendazole and found it to pose a medium risk in river water and a medium to high risk in wastewater for bacteria, and a low risk to Cyanobacteria in both river water and wastewater (Teglia et al. 2025**).

6. Plants

One study found no adverse effect of fenbendazole or flubendazole on the growth of green algae *Scenedesmus vacuolatus* and common duckweed *Lemna minor* (Wagil et al. 2015**).

One study carried out an Environmental Risk Assessment for fenbendazole and found it to pose no risk to plants in river water or wastewater, and a medium risk in river water and a medium to high risk in wastewater for algae (Teglia et al. 2025**).

Narrative Summary of the Studies Retrieved

Boxall et al. 2007* developed a screening-based index for predicting the effects of eight veterinary parasiticides on dung flies. Due to a lack of data, it was no possible to assess the effects of fenbendazole (and oxfendazole) on dung fly populations.

Bundschuh et al. 2016*** quantified the acute toxicity of sulfadiazine, sulfadimidine, flubendazole, fenbendazole, and Ivermectin for nine fresh-water invertebrate species in lab conditions. Fenbendazole and flubendazole had particularly low acute median effective concentrations for *Daphnia magna*, *Dugesia gonocephala*, *Tubifex tubifex*, and *Gammarus pulex*. *D. magna* was the most sensitive species for fenbendazole; *D. gonocephala* and *T. tubifex* for flubendazole. These species may be more effected due to presence and sensitivity of β-tubulin protein subunit. The Predicted No Effect Concentrations for both substances were several orders of magnitude lower than Predicted Environmental Concentrations cited in the literature. This suggests that there is substantial risks for aquatic ecosystems. The Chronic Predicted No Effect Concentration (based on *D. magna* only) showed potential environmental risks for fenbendazole, but not for flubendazole.

Carlsson et al. 2018** tested if exposure to six veterinary antiparasitic pharmaceuticals affects swimming activity of six-day old *Danio rerio*. Fenbendazole exposure did not differ in swimming activity compared to the control group.

Carlsson et al. 2013*** tested the toxicity of fifteen veterinary pharmaceuticals on *Danio rerio*, and the potential metabolism of albendazole, febantel, fenbendazole, and oxfendazole by its embryos in lab conditions. Fenbendazole was among the compounds with the highest observed toxicities. It had one of the steepest concentration-response curves, indicating a small margin between concentrations resulting in no effect and high toxicity. Fenbendazole exposure was associated with abnormal development of the head, eyes, and tail as well as absent circulation and oedema and mortality at higher concentrations. Embryos metabolised fenbendazole into oxfendazole, which is considerably less toxic than the parent drug.

Chen et al. 2021* assessed the occurrence, ecological risk, and exposure evaluation of nineteen anthelmintics at thirty-one river sampling stations and fifteen sediment sampling stations along the Tuojiang River in China. Fenbendazole and flubendazole were found in higher concentrations in sediments rather than river water. There was a significant positive relationship between the pseudo-partitioning coefficient of flubendazole and the Total Organic Carbon content in the sediment, suggesting that the two drugs could partition into sediment rather than water. Environmental risk assessment showed a low risk (risk quotient below 0.1) for flubendazole at all thirty-one river sites, while fenbendazole showed a medium risk at two sites.

Goodenough et al. 2019* studied the lethal and sub-lethal effects of ivermectin, fenbendazole, Pyrantel, and Praziquantel on *Lumbricus terrestris* in lab conditions. Fenbendazole exposure over twelve weeks was associated with a 55% mortality rate. This was the highest mortality rate compared to the other compounds. However, fenbendazole did not have any effect on motility. Fenbendazole does not induce paralysis, but compromises the cytoskeleton. Results are in contrast to previously reported works, possibly because of the concentrations used (0.309 mg/kg dry in standard or 1.547mg/kg dry in high) or the controlled lab environment.

Grønvold et al. 2004* investigated the ecotoxic effect of ivermectin and fenbendazole excreted from bolus-treated cattle on *Pristionchus maupasi* in lab conditions. Fenbendazole had no effect on population growth. At and above concentrations of 10µg per gram of faeces, *P. maupasi* developed significantly smaller population densities. Only at concentrations of 20-25µg per gram of faeces were populations reduced to zero. There was no acute toxic effect in naturally excreted concentrations of fenbendazole, together with its metabolites, in faeces from bolus-treated animals.

Kim et al. 2023* assessed the potential developmental toxicity of flubendazole during neural development using *Danio rerio* as a model in lab conditions. Fenbendazole exposure in aquatic environments reduced the survival rate, hatching rate, and heart rate, and induced pericardial ooedema, yolk-sac ooedema, head and eye deformities, and axial malformations in a concentration-dependent manner. Fenbendazole induced gene-expression changes in the early and late phase of neurogenesis, which caused neural function abnormalities as well as apoptosis and phenotypic malformations in the CNS.

Kim et al. 2010* studied the sorption coefficients of fenbendazole, albendazole, thiabendazole, and flubendazole in lab conditions. Fenbendazole had higher hydrophobicity and therefore strong sorption to dissolved organic components of sewage sludge. This means that fenbendazole is likely to be effectively extracted by conventional wastewater treatment and bound to sludge. However, there may be a higher risk of more of compound bioaccumulating in soil. Flubendazole had a lower hydrophobicity and therefore lower sorption to sewage sludge. This means that it may have a greater likelihood of not being effectively filtered out by sludge treatment and may pose an aquatic exposure risk. However, the sorption and hydrophobicity scores of flubendazole are still relatively high and the study was unable to fully replicate real-world wastewater removal efficiency as it was tested in controlled lab environment.

Kim et al. 2008* developed a prioritisation framework of veterinary pharmaceuticals used in South Korea, based on usage, potential to enter the environment, and toxicological hazard. Fenbendazole was identified as a priority-group compound that warrants immediate attention in environmental monitoring in Korea, as result of high use, high environmental entry potential and high to very high hazard score.

Kumirska et al. 2016** tested water, sediment, and fish tissue at thirteen sampling stations along the river Reda in Poland for fenbendazole, flubendazole, and doramectin. Flubendazole was detected in 12/13 samples, fenbendazole in 11/13, but all were at concentrations below Method Quantification Limit (MQL). Flubendazole and fenbendazole were detected in 2/2 fish samples, but both were below MQL. Flubendazole was detected in 7/13 sediment samples, fenbendazole in 2/13, but all were below MQL. All risk quotients calculated for flubendazole and fenbendazole in water, sediments, and fish tissue were below 1, meaning no risk to the environment For both compounds, the determined concentrations in fish tissue samples were below Maximum Residue Limits in animal tissue, meaning they are safe for consumers.

Oh et al. 2006** quantified the acute aquatic toxicities of albendazole, thiabendazole, flubendazole, febantel, fenbendazole, and oxfendazole through microtoxic assay of *Vibrio fischeri* and acute, chronic, and post-acute exposure-dose responses of *Daphnia magna*. *V. Fischeri* was much less sensitive to anthelmintics than *D. magna*. In acute toxicity tests, fenbendazole had the highest EC_{50} (16.5μg/l); flubendazole the second highest at 48 hours (66.5μg/l). No significant post-exposure delayed effects were detected after three weeks for either compound. Chronic exposure to fenbendazole did not require very high concentrations to have significant negative effect on survival, reproduction and growth (1.25–5.1ppb) and median chronic lethal exposure was 4.1μg/l. For chronic exposure to flubendazole, there was no statistically significant effect on survival, growth, or reproduction at 20μg/l.

Park et al. 2009*** assessed the toxicological effects of fenbendazole on freshwater environments in lab conditions, by examining the molecular and biochemical responses of biomarker genes in *Chironomus riparius* to fenbendazole exposure. There was a significant increase in genes expressing heat shock proteins (indicators of environmental stress) and CYP450 (detoxifies xenobiotics) across all fenbendazole concentrations, in a dose-dependent manner. At the highest concentration (30μg/l), there was a significant reduction in growth and survival rate in larvae, and a significantly increased rate of male emergence and mouthpart deformities in 30μg/l group. Results indicate toxic effects affecting molecular, hormonal, and developmental processes, particularly at higher concentrations of exposure and notably across a 96-hour window (non-significant results at 24 hours).

Podlipná et al. 2013** studied the biotransformation pathways of albendazole and flubendazole in common reed *Phragmatis australis*, using in vitro callus cell cultures, to assess the reed's ability as a potential detoxification tool. Callus cells were exposed to 10μg/l flubendazole and tested over 4, 8, 24, 48 and 96h. Flubendazole was taken up by reed cells, to a point where all its metabolites could be considered inactive, but more slowly and less completely than albendazole. Results suggest a possible mechanism for storing flubendazole metabolites and limiting environmental infiltration and contamination of soil and water.

Puckowski et al. 2017*** evaluated the mixed toxicological effect of fenbendazole and flubendazole on *Daphnia magna*. Single substance results showed high toxicity of flubendazole and fenbendazole towards *D. magna*. Mixtures of flubendazole and fenbendazole were found to cause an effect in accordance with Concentration Addition-based predictions rather than those of Independent Action.

Raisová Stuchlíková et al. 2018** examined the metabolic pathways of fenbendazole and flubendazole in ribwort plantain *Plantago lancelota*, through use of in vitro callus cell cultures. Cells could take up and biotransform flubendazole and fenbendazole into their metabolites. However, most metabolites formed could be decomposed back into active parent compounds. Consumption of ribworts containing metabolites by infected livestock could support drug-resistance development in helminths. Consumption of these ribworts could represent a risk for free-living invertebrates. In the plants themselves, both compounds could cause oxidative stress and decreased antioxidant defense.

Sommer and Bibby 2002** assessed the effect of six veterinary medicines in dung excreted from medicated cows. The mean loss of organic matter was significantly lower in cow dung collected from heifers dosed with fenbendazole. However, significant losses only occurred at 0-16 week period, not at 0-8 or 0-12 weeks. Fenbendazole has a negative influence on the decomposition of dung organic matter in soils, either because it kills detrivores or because of fungicidal activity.

Strong et al. 1996*** analysed the effect of ivermectin and fenbendazole on dung-colonising Coleoptera and Diptera after administering sustained-release boluses to cattle. There were no significant differences in the number of adult beetles found in pats from treated and control groups. The pats from fenbendazole-treated animals contained similar numbers of larval Scarabidae and Diptera compared to the pats from untreated animals throughout the trial. In contrast to Ivermectin, fenbendazole lacks a toxic effect on dung-colonising families of insects.

Stuchlíková et al. 2016** assessed the phytotoxicity and biotransformation of Albendazole, fenbendazole, and flubendazole in harebell *Campanulla rotundiflor*, using in vitro callus cell culture. No acute toxicity of fenbendazole or flubendazole on harebell was detected. Cell viability was not adversely affected by either compound, implying low or no phytotoxicity. Both compounds were metabolised by harebell cells, but not as completely as albendazole (16% of flubendazole after 24h). Most metabolites can be considered deactivation products. However, a number of them remain biologically active. Moreover, a substantial proportion were instable and could easily be decomposed back to the parent anthelmintic.

Svendsen et al. 2002**** studied the effect of faecally excreted ivermectin and fenbendazole (and metabolites) on the survival and growth of the common pastureland earthworm *Lumbricus terrestris* in lab conditions. Fenbendazole and its metabolites had no adverse effects on the survival and growth of *L. terrestris* when exposed through dung under lab conditions.

Svendsen et al. 2003**** compared the disappearance of dung pats from cattle medicated with ivermectin, fenbendazole, and a control group respectively. There was no negative effect of fenbendazole on the biomass of the five most abundant earth worm species (out of eleven). The number and development of dung beetle larvae in pats containing fenbendazole and in control pats were similar. There was no indication of important indirect effects, such as lower attractiveness of dung from treated animals.

Svendsen et al. 2005*** assessed the effects of ivermectin and fenbendazole on earthworm survival, growth, and cocoon production and viability (fecundity), feeding laboratory raised earthworms dung from cattle who had been administered Ivermectin or fenbendazole boluses or from a control group over a two-year period. Fenbendazole did not have a significant effect on growth or survival in first or second generation earthworms raised in laboratory setting, nor did it significantly impact cocoon incubation time or viability.

Teglia et al. 2025** assessed the occurrence of twenty-three emerging contaminants at twenty-three river water stations and ten wastewater stations along the Salado River in Argentina. Fenbendazole detection was among the lowest in river water (4.2% of samples) and among the highest in wastewater (20% of samples). An environmental risk assessment for fenbendazole showed a medium risk for bacteria in river water and waste water, low risk for Cyanobacteria in river water and waste water, medium risk for algae in river water and medium to high in waste water, no risk for plants in river water or waste water, high risk for crustaceans in river water and waste water, low risk to Auran in river water and low to medium in waste water, high risk to fish in river water and waste water.

Van de Steene et al. 2010*** quantified the occurrence of eight pharmaceuticals and one pesticide in waste water and surface water samples. In Waste Water Treatment Plants, concentrations of detected flubendazole ranged widely, but were generally low. Removal efficiencies also varied widely, but generally implied that treatment does not fully eliminate flubendazole from the environment. In surface water, concentrations of flubendazole ranged from below a detectable level to 20.2ng/l. The calculated hazard quotient for flubendazole was below 1 (0.08), meaning that flubendazole posed a low environmental risk.

Wagil et al. 2015** investigated the aquatic ecotoxicity of fenbendazole and flubendazole towards a marine bacterium *Vibrio fischeri*, green algae *Scenedesmus vacuolatus*, common duckweed *Lemna minor*, and *Daphnia magna*. *D. magna* was the most sensitive aquatic organism with a EC_{50} value of 19µg/l for fenbendazole and 45µg/l for flubendazole at 48 hours. No adverse effects on the growth of the algae and duckweed or on the luminescence of *V. Fischeri* up to the highest tested concentration was observed.

Discussion

Results in context

A remarkable finding of this review was that none of the publications or grey literature reviewed contained any direct research on the environmental impacts of fenbendazole and/or flubendazole in UK upland environments in general or as part of grouse-moor management in particular. Instead, all studies either examined the effects of anthelminthics in agricultural systems or simulated the conditions thereof. Comparing results derived from other countries and/or agricultural systems is possible, but, given different species compositions, this needs to be done with certain caveats.

There was strong evidence for the absence of any toxic effect of fenbendazole or flubendazole on terrestrial invertebrates or plants. Research on earthworm species is of limited relevance here, given that peatland soils are generally characterised by the absence of earthworm species. However, research on Coleoptera and Diptera species deserves close attention, as these invertebrate species exist in upland peatland environments and serve as an important food source for the young of many ground-nesting birds, including nationally red-listed wader species.

On the other hand, there was strong evidence for toxic effects of fenbendazole and flubendazole on aquatic environments, especially fish and invertebrates. Studies dedicated to *Daphnia magna* are especially relevant, as this species not only occurs in upland peatland but also serves as an important indicator species for the fate of other invertebrates. Given the high water content of peatland, a negative environmental impact of medicated grit would need to be assumed if the anthelmintics are allowed to leach into water features.

A potential mitigating factor against contamination of water features was highlighted by studies demonstrating high hydrophobicity and sorption to dissolved organic components for fenbendazole and flubendazole (Chen et al. 2021; Kim et al. 2010).[1] Since peatland is characterised by high concentrations of soil organic matter, it can be expected that leached fenbendazole or flubendazole would predominantly bind to soil organic matter rather than water.

Recommendations for grouse-moor management

In light of the observed toxic effect of fenbendazole and flubendazole on aquatic environments, a key objective of sustainable grouse-moor management should be to reduce any risks of the anthelmintics reaching water features.

[1] Similar results were reported by studies not considered relevant for the present purposes (Porto et al. 2021; Kreuzig et al. 2007).

Anthelmintics may potentially enter water features through several routes associated with the use of medicated grit. The most direct pathway may occur where medicated grit is administered directly on the soil, from where it might spill or disperse into nearby water courses, particularly under heavy rainfall, or where grit is placed on sloping ground. Where containers are used, spillage and dispersal are also possible if containers are not secured properly. In addition, faecal excretion by treated grouse may provide a secondary route of contamination, as unmetabolised flubendazole and its metabolites are excreted and may leach or run off into adjacent soils and water bodies. These risks are likely to be greatest where grit is sited close to streams, flushes, or other wet features common in upland environments.

Available best-practice guidance on the use of medicated grit contains several strategies for reducing the risk of water contamination. GWCT (2020) and MMBP (2024) recommend administering medicated grit in small boxes rather than on the bare ground, and placing grit boxes at least 5m away from running and open water. They also advise proper disposal of used grit through professional waste management services.

GWCT (2020) further recommends administering amounts no larger than 500g per grit box. Using single-strength medicated grit, 500g would contain 10g of Flubenvet. Flubenvet in turn contains active flubendazole at a concentration of 5% w/w (DEFRA 2025). A single grit station with 500g of medicated grit therefore contains 0.5g of active flubendazole. As regards leaching rates, Newborn (2007) observed that, on weathered grit, 70% of active flubendazole remains bound to the kernel fat after nine months of being administered. Hence, for 500g of medicated grit, 0.15g of active Flubendazole would potentially leach into the environment over a period of nine months. This is to be considered a low leaching rate, especially given the observations reported above about the hydrophobicity and sorption to organic components of both anthelmintics.

Suggestions for future research

Given the total absence of direct research on the environmental impact of medicated grit in UK upland environments, any new research on this topic is likely to increase our understanding of this topic. At the same time, this review has identified three particular areas of research that would merit further investigation.

The first area concerns the leaching of flubendazole into water features. Though the leaching potential of flubendazole was estimated above to be low, especially where best-practice guidance is observed, the de facto concentrations on grouse moors are entirely unknown. We would propose an empirical investigation into the concentrations of flubendazole in water samples from sites where medicated grit is administered compared to sites where it is not. Such an investigation would allow an adequate quantification of the environmental risk of medicated grit on upland environments. It would also provide a robust evidence base for adjusting, if required, current best-practice guidance.

A second area concerns the metabolisation of flubendazole in red grouse. Several studies included here investigated the concentrations and effect of fenbendazole or flubendazole excreted in the faeces of domesticated mammals such as cows, pigs, or sheep (Grønvold et al. 2004; Sommer and Bibby 2002; Strong et al. 1996).[2] Faecal excretion of flubendazole by red grouse is assumed above to be a potential pathway of environmental contamination. The extent of such contamination, however, is unknown and the results of studies derived from agricultural systems are of limited relevance because of differences in drug administration and host digestive systems. We would propose a laboratory analysis of the faeces of red grouse from sites where medicated grit is administered compared to sites where it is not.

A third area concerns the fate of the compounds in plants. Podlipná et al. (2013), Stuchlíková et al. (2016), and Raisová Stuchlíková et al. (2018) showed that fenbendazole and flubendazole were biotransformed in the cells of certain plants. They cautioned that some metabolites remained biologically active, while others could potentially be decomposed back to the parent anthelmintic within the digestive system of herbivores. Both scenarios might contribute to the build-up of a resistance of strongyle worms to the anthelmintics, if infested animals ingest these plants, and affect free-living invertebrates, either directly or after excretion of the anthelminthic by animals. For UK uplands, the biotransformation pathways of dominant plant species, such as *Calluna vulgaris* or *Eriophorum vaginatum*, are currently unknown. If sustainable grouse moor management is to avoid unintended effects on non-target species and resistance build-up in target species, it would be helpful to better understand the biotransformation of flubendazole in moorland plants. We would propose a laboratory analysis of samples from key moorland species collected on sites where medicated grit is administered compared to sites where it is not.

Limitations

In this report, we applied a Rapid Evidence Assessment approach that sought to identify relevant literature in an objective, transparent and repeatable way with minimal bias. This approach seeks to balance returning a comprehensive versus manageable list of candidate studies. Querying large databases with defined search strings seemed the best way to achieve this objective, and Web of Science and Scopus were chosen as they seemed to contain the majority of peer-reviewed journal articles and book sections.

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[2] Similar effects are studied by a number of studies not included here (Kreuzig et al. 2007; Porto et al. 2021; Rakonjac et al. 2022; Weiss et al. 2008).

This approach involved two risks. First, within the databases queried, relevant literature might be omitted if their titles, abstracts, or keywords do not match the terms of the search string. Second, no comparable databases could be found for formats of scientific research other than peer-reviewed journal articles and books sections, as for instance reports.

We aimed to control these risks by two means. First, we designed the search strings as economically and broadly as possible. It is hard to conceive of a study dedicated to fenbendazole or flubendazole that does not mention the name of the compound in either title, abstract, or keywords. We found that even studies examining large groups of veterinary pharmaceuticals tend to list them individually in the abstracts. Second, we checked the reference lists of all papers included in this review for relevant literature that had been omitted by the searches. We found that only one relevant study (Chen et al. 2021) had been omitted by the database searches.

We are confident that these two strategies have allowed us to capture, if not the totality, at least a representative majority of all relevant scientific literature on this subject.

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