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Potential environmental consequences of administration of anthelmintics to sheep

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ABSTRACT

Anthelmintics, veterinary medicines for the control of endoparasites, enter into the environment largely through faeces of the treated animals. Sheep dung is a patchily distributed, ephemeral resource, with a functionally important decomposer community. The nature of this community and the pharmacokinetics of anthelmintics in sheep mean that the ecotoxic impacts of these drugs in sheep dung may differ markedly from those in cattle dung, where most research has been focussed. The period of maximum residue excretion is generally more transient in sheep than cattle dung, but low-level excretion may continue for longer, giving the potential for extended sub-lethal effects. Here, the environmental impacts of sheep anthelmintics, as well as alternative endoparasite control methods are reviewed. Impacts are discussed in terms of the potential for residues to enter into the environment, the toxicity and the impact on ecosystem functioning at an appropriate scale. Future research priorities are also discussed; these include the need for studies of the functional contributions of dung-colonising species, as well as the development of higher-tier ecotoxicological methods bridging the gap between laboratory and field experiments. Large-scale and long-term studies, including the development of appropriate models, are necessary to allow the consequences of anthelmintic administration to be assessed, particularly within the remit of sustainable animal production.

1. Introduction

The control of internal parasites is vital for sustainable sheep production; however, it comes at a cost. For example, internal parasite control costs the UK sheep industry about GBP 84 million annually (Nieuwhof and Bishop, 2005). Sheep anthelmintics, veterinary medicines that control gastro-intestinal helminthes, liver fluke and lungworms (Floate et al., 2005), may be applied topically, orally, *via* intraruminal boluses, by injection or in-feed. Anthelmintics administered to sheep enter into the environment primarily through their excretion in faeces (Halling-Sørensen et al., 2001); for example, >98% of ivermectin (regardless of route of administration) is excreted in faeces (Halley et al., 1989a). However, the precise excretion profile is linked to the mode of administration (Boxall et al., 2003). Pour-on administered drugs are excreted largely unaltered in the faeces, whereas compounds administered orally or by injection are metabolised to a greater degree prior to excretion (Wardhaugh, 2005). The exceptions are the benzimidazoles, imidazothiazoles and tetrahydropyrimidines, which are mainly excreted in urine (McKellar, 1997). The wash-off of topically applied compounds from the fleece, spillage during application and inappropriate disposal of compounds provide other important environmental entry points (Boxall et al., 2002). Contamination is not limited to soil and dung; drugs may leach into groundwater and reach water-bodies through surface run-off or be excreted or washed-off treated animals directly into a watercourse (Boxall et al., 2002). The entry of anthelmintics into the environment due to the manufacturing process is likely to

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be low in the European Union (EU) or the USA, due to stringent manufacture and formulation regulations. For other countries, this contribution is largely unknown (Boxall et al., 2003).

Here, the potential ecotoxic impacts of anthelmintics administered to sheep for the control of internal parasites are considered (Table 1). An evaluation of the environmental impact of alternative products marketed for parasite control is also included, where sufficient data allows. Studies of cattle dung are not reviewed systematically here and are referred to only where required to highlight differences in excretion and ecotoxicity between sheep and cattle.

2. Ecotoxicity tests

Ecotoxicity tests have been required for veterinary medicines by the EU since the early 1990s and by the U.S. Food and Drugs Administration (FDA) since 1980 (European Commission, 1992; Boxall et al., 2003). Discussions for new guidance documents are underway, involving EU countries, the USA and Japan, with Australia, New Zealand and Canada as observers (VICH, 2004). Current ecotoxicity tests focus on fish, daphnids, algae, microbes, earthworms, plants and dung invertebrates. The Environment Agency of England and Wales uses the results from a targeted monitoring study of veterinary medicines to assess potential ecotoxic impacts of veterinary medicines, with information gathered from the United Kingdom, Germany, the Netherlands and Denmark (Boxall et al., 2006). The majority of sheep anthelmintics are classified as high possible impact, with high usage/impact products also identified as such in other countries (Jorgensen and Halling-Sørensen, 2000).

The main focus of study for the ecotoxic effects of anthelmintics has been the macrocyclic lactones (MLs), in particular ivermectin. Lumaret (1986) was the first to suggest a field impact of ivermectin on cattle dung fauna, with Wall and Strong (1987) finding an associated retardation of dung decomposition. Since then, many studies, both in the field and in the laboratory, have confirmed this. The wide spectrum of activity of ivermectin against endo- and ectoparasites increases the potential for impacts on non-target organisms. As ivermectin may be stored for long periods in soil (Mougin et al., 2003), impacts on soil fauna have also been comprehensively assessed. More recently, work has focussed on single- or multi-species laboratory toxicity tests, where coprophagous fly and dung beetle larvae are particularly sensitive (Hempel et al., 2006; OECD, 2007, 2009; Römbke et al., 2007a,b, 2009a,b). Earthworms appear to be less sensitive to residues, but with possible sub-lethal effects on some species from exposure to abamectin (Diao et al., 2007; Jensen et al., 2007). Toxic and sub-lethal effects of abamectin, doramectin and ivermectin have been reported on collembolans and predatory mites (Römbke et al., 2010), enchytraeids (Jensen et al., 2003) and isopods (Kolar et al., 2010); impact of ivermectin on soil fauna feeding rates has also been reported (Förster et al., 2011). However, the impact of residues excreted in urine on soil biota is still largely unknown (McKellar, 1997).

Macrocyclic lactone residues have been found in aerobic water sediments (Prasse et al., 2009) and have been shown to be toxic to a number of aquatic invertebrates (OECD, 1984, 1998; Burridge and Haya, 1993). This raises concerns over the possible non-target aquatic impact of anthelmintics, from incorrect disposal, fleece wash-off or faecal/urinary contamination of water courses. MLs have not been shown to exhibit antifungal, antibacterial, antiprotozoal and anti-algal effects in the laboratory (Halley et al., 1989a; Escher et al., 2008) or at field concentrations, with no impact on soil microbe nitrification and respiration (Halley et al., 1989a,b). However, there may be a long-term effect of ivermectin to the soil fungus *Fusarium oxysporum*, where both production and germination of spores were reduced after exposure; in contrast, spore production doubled in *Phanerochaete chrysosporium* and *Mucor racemosus* (Kollmann et al., 2003). However, the concentrations used in the latter study were far higher than predicted soil or dung concentrations. It is widely accepted that benzimidazoles have a fungicidal effect (Araujo et al., 1995; Sanyal et al., 2004). Decomposition of cattle dung in soil has been shown to be retarded by both levamisole and fenbendazole (Sommer and Bibby, 2002), but this has not been directly linked to a fungicidal impact.

The benzimidazoles and imidazothiazoles have received some coverage in the literature, showing little ecotoxic impact to dung or soil fauna. Similarly, literature on the ecotoxic impact of hexahydropyrazines, tetrahydropyimidines and aminoacetonitrile derivatives is limited to one or two studies for each group. Laboratory studies have recorded no effects of praziquantel on dung beetles (Hempel et al., 2006) and no effects of morantel on soil mesofauna (Jensen et al., 2009). There appear to be no independent ecotoxicity studies on the salicylanilides, the diphenylsulphides, clorsulon, pyrantel embonate or tetramisol. Various aspects of similar effects of anthelmintics on dung, soil and aquatic fauna after administration to cattle have been described by Strong (1992, 1993), Herd and Wardhaugh (1993), McKellar (1997), Spratt (1997), Wardhaugh and Ridsdill-Smith (1998), Floate (1999), Lumaret and Errouissi (2002), Suarez (2002), Boxall et al. (2003), Floate et al. (2005), Floate (2006) and Schmitt and Römbke (2008). However, the environmental impact of anthelmintics after administration to sheep is less well-known.

3. The sheep dung decomposer community

The ecology, as well as functional and economic importance of cattle dung communities on dung decomposition, parasite bio-control, pasture fertility, soil health and as prey for higher vertebrates have been well documented and reviewed (Landin, 1961; Bergstrom et al., 1976; Fincher, 1981; Anderson et al., 1984; Hanski, 1991; Gittings et al., 1994; Ward and Wilhelm, 1994; Spratt, 1997; Manfredi, 2006; Yamada et al., 2007; Nichols et al., 2008; Rosenlew and Roslin, 2008; d'Alexis et al., 2009; Wall and Beynon, 2012). Indeed, the ecosystem function of dung decomposition in agricultural grasslands has been identified as one of the key questions of high policy relevance in the UK (Sutherland et al., 2006). However, the ecology of sheep dung decomposing communities is much less well known.