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**Review article**

# Use of anthelmintics in herbivores and evaluation of risks for the non target fauna of pastures

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**Abstract** – The overall purpose of this paper was to review the major and most recent literature relating the effects of anthelmintics on dung breeding invertebrates and dung degradation. Faecal residues or metabolites of drugs belonging to the benzimidazole and levamisole/morantel groups are relatively harmless to dung fauna, on the contrary to other anthelmintics such as coumaphos, dichlorvos, phenothiazine, piperazine, synthetic pyrethroids, and most macrocyclic lactones which have been shown to be highly toxic for dung beetles (abamectin, ivermectin, eprinomectin, doramectin), among which moxidectin was the less toxic for dung beetles. To date, the detrimental impact upon non-target organisms has been considered acceptable in eradicating the parasites because of their economic importance to commercial livestock production. The consequences of routine treatments are discussed with consideration of the long-term consequences for cow pat fauna and sustainable pastureland ecology.

**anthelmintic / residue / dung beetle / Diptera / sustainable parasite control**

**Résumé – Usage des anthelminthiques en élevage et évaluation des risques pour la faune non cible du pâturage.** Cet article de synthèse passe en revue les travaux de la littérature les plus récents concernant les effets secondaires des principaux produits vétérinaires utilisés en routine sur la faune coprophage et sur la dégradation des excréments dans les pâturages. Les résidus (ou les métabolites) des groupes du benzimidazole et levamisole/morantel trouvés dans les excréments s'avèrent relativement peu toxiques pour la faune coprophage. Au contraire les anthelminthiques des groupes suivants s'avèrent hautement toxiques: coumaphos, dichlorvos, phénothiazine, pipérazine, pyréthroïdes de synthèse, et la plupart des lactones macrocycliques (abamectine, ivermectine, éprinomectine, doramectine), la moxidectine étant la moins toxique pour la faune coprophage. Jusqu'à présent, cet impact négatif a été considéré comme acceptable par les éleveurs et firmes pharmaceutiques en regard de l'importance économique du contrôle et/ou l'éradication des parasites. Les conséquences des traitements de routine sont discutées en considérant que l'absence de dégradation des bouses constatée

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localement peut malgré tout s'accompagner d'une érosion silencieuse de la biodiversité, avec un déséquilibre à long terme du fonctionnement des pâturages.

**anthelminthique / résidus / coléoptère coprophage / diptère / contrôle raisonné des parasites**

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## 1. INTRODUCTION

Over the past decade, concerns have been increasingly expressed by the scientific community regarding the possible unintended side effects of chemicals used in veterinary and agricultural practices and, more particularly, in the widespread use of the macrocyclic lactone class of chemicals such as anthelmintics used to control gastrointestinal parasites of grazing livestock and companion animals. In the scientific community there is a lack of consensus over the potential of macrocyclic lactone residues, excreted in the dung of treated animals, to harm dung beetles that utilise this dung. Scientists do not agree on the extent of such risks, mainly because of the complex dynamics of insect populations that fluctuates widely according to factors such as climatic fluctuations, rainfall, cattle management and pasture quality [6, 98]. This situation has raised concerns not only for the possible impact on dung degradation but also for the consequences on pastureland insect communities and ecosystem stability and on the sustainability of pasture fertility [8, 41, 50, 64, 68, 81, 107, 115, 117]. At the same time, it has been shown that modern anthelmintics also adversely affect the development and survival of non-target organisms in estuarine and marine ecosystems [17, 18, 23, 36, 37].

The development of anthelmintics and latterly endectocides with a broad range of target pathogens has provided more efficient and economic options for the treatment and control of parasitic disease both in ruminant and monogastric animals. In pastures, most antiparasitic agents are excreted, to some extent, in the faeces of treated animals, creating a concern for their effect on the organisms that feed and/or breed in animal excrements. As the spectrum of activity of the antiparasitic agents has enlarged, the potential for affecting non-target organisms has increased equally [81]. Many of the non-target organisms play a vital role in the processes of dung dispersal. They are crucial for maintaining pasture hygiene, nutrient cycling, soil aeration, humus content, water percolation and pasture productivity. In addition, they also ensure that the livestock grazing area is not drastically reduced by an accumulation of dung [50]. In the cow dung community, dung feeder flies [42], coprophagous beetles [43, 44, 53] and annelid worms [54, 55, 85] are the most important organisms. Under warm and dry climate conditions, dung beetles appear the most important organisms to degrade dung pats, while earthworms predominate both in activity and biomass under temperate and more mesic conditions [85]. Earthworms aggregate under dung pats [15] and it has been demonstrated that dung is readily eaten and removed from the surface by these organisms which are therefore presumed to play an important role in the decay and disappearance of dung [38]. However, it has been shown that earthworm activity in pats may strongly depend on beetle occurrence and activity. Beetles rapidly colonise and oviposite in dung pats in the first few days after they are dropped, facilitating the initial breakdown of dung and allowing the subsequent entry of earthworms which continue to degrade the dung [15, 38, 55, 107]. The occurrence of many species is facilitated by the activities of other species which colonise droppings earlier. When beetles utilise dung pats, they dig small tunnels which weaken the pats and, at the same time, beetles inoculate the heart of pats with microorganisms as they carry spores of telluric fungi and microorganisms on their integument. Consequently, the presence of beetles stimulates the microbial activity. Normally, about 80% of the ammonia release from dung pats is lost during the first five days, but when sufficient numbers of beetles are present for quick burial, the loss is reduced to 5–15% and permits the use of this N by plants for up to two years. Under such conditions, pats become progressively soil annexes, with the network of tunnels making colonisation of pats by edaphic fauna easier [25]. Tunnels made by beetles improve the oxygen supply to coprophagous flies but also provide runways so predatory Staphylinids can get at the flies [105]. Dung burial by beetles decreases wastage of herbage through the rejection of fouled herbage and smothering of pasture leaf area [68].

There is now a considerable amount of data on the risks of the adverse effects of some anthelmintics on non-target invertebrates. Faecal residues or metabolites of drugs belonging to the benzimidazole and levamisole/morantel groups are thought to be relatively harmless to dung fauna [81, 110], on the contrary to other anthelmintics such as coumaphos, dichlorvos, phenothiazine, piperazine [12, 64], synthetic pyrethroids [10, 115], and most macrocyclic lactones [25, 50, 99, 100, 102] which have been shown to be highly toxic for dung beetles.

Several factors can modify the environmental risks: (i) The amount of the active agent which enters the environment; this amount depends on the route or delivery system of administration [50], and on the physiology of the treated animals [3, 4]; (ii) The concentration and persistence of the drug in the faeces, and the total amount of droppings from treated animals compared to the total faecal deposits in the pasture [30, 81]; (iii) Environmental factors (light, rainfall, temperature…) and the coincidence of deposits with activity of non-target organisms [30, 41]; (iv) The susceptibility of organisms, some taxa are more susceptible than others, and some are highly resistant [24, 25, 28, 29, 35, 39, 41, 112, 113].

In the present paper, the environmental effects and fates of anthelmintics are reviewed from data collected for the registration of some compounds and from scientific literature.

## 2. PHARMACOKINETICS AND ROUTES OF ELIMINATION

In a recent and exhaustive report, Wardhaugh [110] reviewed the parasiticides registered for use in cattle in Australia. The author gave information on the excretion route and insecticidal activity of particular chemicals and cites literature that contains relevant information. The main delivery routes of these parasiticides are oral, pour-on, injectable, sustained-release bolus, back-liner, back-rubber, back-spray, and ear tag. Endectocides (e.g. abamectin, moxidectin, doramectin, ivermectin, and eprinomectin) are mostly delivered through injectable, sustained-release bolus and pour-on, while the delivery routes of ectocides are more diverse.

Levamisole and albendazole are mainly eliminated in the urine [12, 47, 86], while the principal elimination route of oxfendazole, fenbendazole, and morantel concerns the faeces, without significant insecticidal activity on non-target fauna [46, 48, 64, 82, 103]. Macrocyclic lactones are primarily excreted in the faeces, with noticeable insecticidal activity on non-target organisms. This concerns abamectin [56, 86, 88], ivermectin [14, 29, 59, 68, 88, 96, 103, 107, 112], eprinomectin [109, 117], doramectin [32, 93, 98] and moxidectin [28, 58, 98, 101, 109, 114, 120]. Insecticidal activity in the faeces was noticed with synthetic pyrethroids (alpha-cypermethrin [10, 11], flumethrin [10], cypermethrin [10, 11, 61], deltamethrin [10, 33, 106, 115], cyhalothrin [10, 11], permethrin [33], fenvalerate [91]) and organo-phosphates, e.g. dichlorvos [64]. Other chemicals used in cattle also showed insecticidal activity in faeces, e.g. diflubenzuron [26], clorsulon [104], triflumuron [83] and methoprene [26].

Injectable or subcutaneous formulations of endectocides promote a slow absorption of the drug from the subcutaneous injection site to produce an effective controlled release formulation [63] and to extend the period of high plasma concentration [50]. Intramuscular injection of ivermectin is an oil-based formulation, which increases the lipophilicity of the drug and promotes a slow release from the injection site and a longer mean residence time in the animal when compared to other formulations. Topical pour-on formulations of endectocides are alcohol-based formulations and they are mainly administered using a high dosage. A higher ivermectin concentration has been reported in cattle dung, when a topical pour-on formulation was used as compared with an injectable formulation; however both formulations showed comparable persistency [95]. Sustained-release bolus mostly concerns ivermectin, morantel and benzimidazoles. According to the manufacturer, each bolus of ivermectin given to a 150–450 kg calf contains 1.72 g of the active molecule which is released by an osmotic pump at a rate of about 12 $mg \cdot day^{-1}$ over 135 days. The high levels of ivermectin recovered in cattle faeces indicate that a large proportion of the dose released by the bolus (80 to 90%) is excreted in the faeces [4]. This route of administration and elimination is potentially more disruptive to the pasture ecosystem than any other formulation because of their slow release and extended period activity [53]. Ivermectin is not metabolised in the rumen and a significant part of the drug may pass down the gastrointestinal tract into the faeces without absorption into the systemic circulation [5]. Oral formulations (oral paste or drench formulations) of ivermectin for sheep and horses have less bioavailability and persistence than the injectable formulation for cattle [50, 65, 76]. Herd [50] estimated that this formulation had fewer environmental effects, although the use of an oral paste for horses still resulted in a significant delay in dung degradation rates [52].

## 3. CONCENTRATION, STABILITY AND ACTIVITY OF ANTHELMINTICS IN THE FAECES; EFFECTS ON NON-TARGET DUNG-FEEDING FAUNA

In laboratory studies, dung from sheep treated with an oral mixture of oxfendazole and levamisole was shown to be toxic to both fly and beetle larvae [113]. The mortality was thought to be associated with the oxfendazole component since levamisole is rapidly absorbed following oral, subcutaneous or topical administration, and is rapidly and largely excreted unchanged in the urine. However in field studies, using a pulse release formulation delivering 750 mg of oxfendazole, no evidence of any effects of oxfendazole on the rate of dung degradation or on the numbers or weight of earthworms in the pasture were found [119]. According to McKellar [81], the benzimidazoles have relatively short residence times following single oral administration and very low concentrations are passed in the faeces within 36 h (thiabendazole), 96 h (albendazole) or 168 h (oxfendazole, fenbendazole) after administration [73–75, 118]. The fenbendazole bolus delivers 67–103 mg of fenbendazole per animal per day with prophylactic activity for 140 days [89].

The relative daily doses of morantel are 680–2300 mg per animal (oral drench) and 50–150 mg per animal (sustained-release bolus) [13]. Twenty-four hours after oral administration of morantel tartrate (which is poorly absorbed following oral administration) at 10 $mg \cdot kg^{-1}$ bodyweight, the concentration of morantel in the faeces collected from cattle were > 10 $\mu g \cdot g^{-1}$ (dry weight) [82]. Morantel did not affect the development of the yellow dung fly in the faeces from treated cattle [82].

When cattle were treated with the pyrethroid flumethrin pour-on at the recommended dose (1 $mL \cdot 10\ kg^{-1}$), the results indicate that flumethrin did not affect the degradation of the dung pats exposed in the field 1–28 days after treatment compared with the pats of the control group [60]. However this result is not consistent with the findings of Bianchin et al. [10] on the lethal effects of flumethrin residues in faeces on adult dung beetles of *Onthophagus gazella*, a species also present in the previous trial area: field observations made by farmers showed beetles dying after application of the parasiticide [60]. Wardaugh et al. [115] showed that residues of deltamethrin (pour-on formulation) in cattle dung were excreted in concentrations sufficient to inhibit survival of larvae of the dung-breeding fly *Musca vetustissima* for 7–14 days after treatment. Peak concentrations of 0.4 mg deltamethrin$\cdot kg^{-1}$ dry weight of faeces occurred three days after treatment and were sufficient to kill adult beetles (*Onthophagus binodis* and *Euoniticellus fulvus*) for at least twice this period.

Studies on the potential ecotoxic effects of endectocides in the environment showed that these effects depend on animals (cattle, horses, sheep), the formulation or delivery system in which endectocides are administered, and the stages of the non-target organisms (either adults or larvae). Ivermectin concentrations in faeces decline with time from approximately day 2 after subcutaneous or pour-on administration. Following the administration of 300 $\mu g \cdot kg^{-1}$ by the subcutaneous route, concentrations of ivermectin in the faeces declined from 8 $\mu g \cdot g^{-1}$ on day 2 post-administration to approximately 2.5 $\mu g \cdot g^{-1}$ by day 7 post-administration [19]. Following administration to cattle of a sustained-release bolus prepared to deliver ivermectin at a low daily dosage for 135 days, the faecal ivermectin concentration dropped to a steady-state concentration of around 1.18 $\mu g \cdot g^{-1}$ which was maintained up to 120 days post-treatment [4]. Ivermectin was detected in both plasma (0.05 $ng \cdot mL^{-1}$) and faeces (2.67 $ng \cdot g^{-1}$) up to 160 days. This faecal excretion of high ivermectin concentrations for prolonged periods after bolus administration to cattle may represent a special threat to the ecosystem.

In horses, the comparison of the faecal excretion profile of moxidectin and ivermectin after oral administration showed that ivermectin remained above the detectable level for 40 days (0.6 ± 0.3 $ng \cdot g^{-1}$), whereas moxidectin remained detectable for 75 days (4.3 ± 2.8 $ng \cdot g^{-1}$) [84]. Ivermectin presented a faster elimination rate than moxidectin, reaching 90% of the total drug excreted in the faeces at four days post-treatment, whereas moxidectin reached similar levels at eight days post-treatment. No significant differences were observed for the values of maximum faecal concentration (C max) and time of C max between both groups of horses, demonstrating similar patterns of drug transference from the plasma to the gastrointestinal tract. The values of the area under the faecal concentration time curve were slightly higher in the moxidectin treatment group (7 104 ± 2 277 ng·day·g$^{-1}$) but were not significantly different from those obtained in the ivermectin treatment group (5 642 ± 1 122 ng·day·g$^{-1}$). The concentration in the faeces only represented 44.3 ± 18.0% of the total parental drug administered compared to 74.3 ± 20.2% for ivermectin. This suggests a higher level of metabolization for moxidectin in horses [84].

Studies on the potential ecotoxic effects of endectocides led intense interest in elucidating the fate of these drugs in the faeces [4, 25, 28, 50, 66, 107, 112, 113]. The environmental impact of antiparasitic chemotherapy depends on the deleterious effects which the agent or its metabolites have on an organism in the locus of excreta, the amount of the active agent excreted, the temporal nature of excretion and the stability of the ecotoxic residues [81]. The faecal concentration levels of ivermectin found in horse droppings [84] were all above concentrations that are lethal or sublethal to many dung breeding invertebrates of benefit to the ecosystem [50, 100]. It has been demonstrated that ivermectin concentrations as low as 0.001 μg·g$^{-1}$ (1 ng·g$^{-1}$) wet weight are toxic to some dung breeding insects [101].

Although greater persistence of faecal excretion was obtained in the horses treated with moxidectin, these results do not necessarily signify that moxidectin is more ecotoxic than ivermectin, particularly on the dung degradation fauna [50]. Probably, the main differences between moxidectin and ivermectin are related to physicochemical differences that explain their pharmacokinetic and metabolic characteristics [84].

The differences observed in anthelmintic efficiency between both drugs can be extrapolated to their environmental impact on dung fauna. According to Herd [50] the experiments reported in several countries indicate that moxidectin is ecologically safer than ivermectin. It has been reported that 200 μg·kg$^{-1}$ b.w. of moxidectin in cattle had no adverse effects on adult emergence of the dung beetles *Onthophagus gazella* and *Euoniticellus intermedius*, whereas ivermectin residues in the faeces significantly reduced the adult emergence [28]. Moreover, a comparative study carried out on steers [114] demonstrated that dung residues in the faeces collected 3–35 days after treatment with an injectable formulation of moxidectin (200 μg·kg$^{-1}$) had no significant effects on the survival of larvae of *Musca vetustissima* or *M. domestica*. In contrast, ivermectin treated steers produced dung that inhibited larval development of both *M. vetustissima* and *M. domestica* for a period of 14 days after treatment.

In horses, Lumaret [66] demonstrated significant adverse effects on the fly *Neomyia cornicina* for five days after oral treatment with moxidectin administered in doses of 400 μg·kg$^{-1}$ whereas the administration of a dose of 200 μg·kg$^{-1}$ of ivermectin had effects for 21 days. These differences could explain why moxidectin can attain prolonged and persistent concentrations in faeces although its environmental effects may be shorter than those observed in ivermectin treated animals.

In sheep, the oral administration of moxidectin results in initial faecal concentrations that are 10 times higher than those observed in cattle after subcutaneous injection, but by seven days the levels in both sheep and cattle are similar. At this stage, the cumulative excretion accounts for 43%

of the dose and parent moxidectin comprises 25% of the total residues in sheep faeces [1]. The faecal excretion of orally administered ivermectin by sheep is more rapid. By seven days, the faecal residues account for 69% of the dose and 61–69% of these residues are present as the parent drug [40, 76]. Other studies have shown 95% recovery of the total dose in the faeces of sheep seven days after intra-ruminal administration [2], two-thirds of this being recovered during the first two days [98]. The presence of ivermectin residues in sheep droppings after oral administration influenced the survival of fly and beetle larvae for less than a week after treatment, but such transient effects were unlikely to have a major impact on insect populations [113]. However, the recent introduction of controlled-release capsules of ivermectin for sheep have modified previous conclusions [116]. The capsule releases a measured amount of ivermectin each day and operates for 100 days. No fly larvae and almost no beetle larvae survived in sheep faeces collected up to 39 days after capsule administration. Newly emerged *Onthophagus taurus* (Coleoptera: Scarabaeidae) also suffered significant mortality whereas those who survived underwent delayed sexual maturation [116]. Ivermectin residues had no effect on the survival of sexually mature beetles, but reduced the fecundity of *O. taurus*.

In most cases, the mortality of sexually mature adults was unaffected although an increased mortality and a slower rate of ovarian development were recorded in the newly emerged dung beetle *Onthophagus binodis* feeding for an extended period of eight weeks on the dung of cattle treated with abamectin [86]. Similarly, an increased mortality of newly-emerged *Copris hispanus* and *Onitis belial* adults has been recorded after feeding for 14 days on dung containing ivermectin residues collected up to eight days after treatment [112]. *Copris hispanus* displayed a suppressed feeding activity and females had a greatly reduced fat accumulation and distended guts with unusual contents after feeding for 43 days on dung collected after ivermectin treatment [112]. Ivermectin residues in sheep dung also increased the mortality of newly emerged *Euoniticellus fulvus* when feeding for 10 days on faeces voided during the first day after drenching, but not subsequently [113]. Conversely, sexually mature adults of *Anoplotrupes stercorosus* (Col. Geotrupidae) feeding on horse droppings collected immediately following oral ivermectin treatment showed no apparent toxicological effect [65].

On the contrary to adults, the larval stages of dung beetles are highly susceptible to avermectin residues in cattle and sheep dung. An increased larval mortality, in many instances up to 100%, has been observed in dung collected during the first weeks or months after treatment [98]. Delayed larval development has been recorded in *Onthophagus gazella* [27, 86, 94], whilst the morphology of the head capsules of dead larvae indicated that toxicity occurred at the first instar stage; the examination of surviving third-stage instars from day seven dung indicated sub-lethal effects of ivermectin residues [94]. The effects of cattle treatment (two trials) with ivermectin slow-release (SR) bolus were monitored on the larval development of the dung beetle *Aphodius constans* Duft. (Col. Aphodiidae) [25]. In the first trial, faecal ivermectin concentration reached a peak at 63 days post-treatment (1 427 $ng \cdot g^{-1}$) and ivermectin was detected up to 147 days post-treatment (7.2 $ng \cdot g^{-1}$). In this trial, ivermectin prevented the development of larvae *A. constans* (100% mortality) until day 105, while at day 135 the rate of emergence was still significantly lower than the control. In the second trial, the difference between the control and the treated series remained significant until 143 days post-treatment, with no emergence until 128 days post-administration of the SR bolus to cattle [25].

The toxicity of macrocyclic lactone residues to the development of eggs and larvae of dung breeding flies has been extensively examined, since many species are considered as pests. The larval development of the house fly *Musca domestica* and the bush fly *Musca vetustissima* are significantly affected for up to four weeks after subcutaneous ivermectin treatment of cattle (0.2 $mg \cdot kg^{-1}$) [70, 86, 113, 114]. Adult females of the sheep blowfly *Lucilia cuprin*a exhibited impaired ovarian development, reduced fecundity and reduced survival when fed continuously on sheep dung collected within 24 hours of oral treatment with ivermectin, whereas adult males showed aberrant mating behaviour [20, 21, 71, 72]. The face fly *Musca autumnalis* showed a 14–46 day period of reduced larval development [70, 96], on the contrary to the stable fly *Stomoxys calcitrans* where less toxic effects were observed after subcutaneous ivermectin treatment of cattle [90]. The effects of ivermectin on *Neomyia cornicina*, an obligate dung feeder, show similar differences between cattle and sheep faecal residues, with larval development being reduced for up to 32 days and 7 days, respectively, and with physiological modifications [34, 35, 96, 112]. By contrast, dung collected as early as three days after the subcutaneous treatment of cattle with moxidectin had no effect on the development of *M. domestica* and *M. vetustissima* larvae [24, 114]. In addition, following oral moxidectin treatment, residues in sheep faeces were toxic to *N. cornicina* development for a shorter period than those following oral ivermectin treatment [66].

## 4. INFLUENCE OF ANTHELMINTICS ON DUNG DEGRADATION

The recycling of faeces is a complex linkage of slow processes in which microorganisms and the edaphic fauna intervene at the soil surface as well as in the upper layers of the soil, where climatic conditions influence the activity of dung-breeding insects (Scarabaeidae, Hydrophilidae, Staphylinidae, larvae of Diptera) [67]. When beetles exploit dung pats, they dig small tunnels, which weaken the pats and, at the same time, beetles inoculate the heart of pats with microorganisms as they carry spores of telluric fungi and microorganisms on their integument. Consequently, the presence of beetles stimulates the microbial activity [16, 69]. It is also well known that the dung-breeding Diptera assists in breaking down cattle dung pats [45]. Under such conditions, pats progressively become soil annexes, the network of tunnels making the colonisation of pats by edaphic mesofauna easier. The artificial exclusion of both flies and beetles from fresh cattle dung pats for only one month after the deposition of pats considerably lowers the rate of decay [67].

The alteration in the rate of degradation has not been reported for faeces from animals treated with benzimidazole, levamisole and oxibendazole [52]. Krüger et al. [60] indicated that the fluomethrin did not affect the degradation of dung pats exposed in the field 1–28 days after treatment of cattle compared with pats of a control group. By comparison, Lumaret [64] investigated the impact of dichlorvos treatment of horses on dung degradation. Artificial faecal copromes using dung collected two days after treatment disintegrated more slowly than those from untreated horses (57% and 0% remanence respectively, after an eight-month exposure in the field). Herd et al. [52] also reported a significant delay in dung dispersal when horses were treated with ivermectin. By the end of their study (eight months), there was a 24.7% reduction in ivermectin copromes compared with 59.1% and 59.9% for control and oxibendazole copromes, respectively. In addition, there were significantly more copromes showing complete dispersal in oxibendazole or control plots than in ivermectin plots.

In Great Britain, in one trial in which cattle were dosed with an experimental sustained-release bolus delivering eight mg of ivermectin daily, the faeces were shown to be highly toxic to dung feeding insects, the absence of which significantly retarded the rate of dung pat degradation [107]. Dung from cattle treated with ivermectin was solid and intact after 100 days due to non dung beetle activity. In Denmark, Madsen et al. [70] showed that the decomposition of dung pats from recently ivermectin treated heifers was delayed within the first three weeks when compared with a control. However no adverse effects of treatment were recorded on earthworms and the retarded decomposition rate was ascribed to the adverse effects on the primary dipteran decomposing fauna. Similarly in Canada, Floate [29] reported that insect activity was significantly reduced in dung from cattle treated with a recommended dose (500 $\mu g \cdot kg^{-1}$) of ivermectin. Reduced insect activity was associated with slower dung pat degradation. When ivermectin was added directly to the dung, at levels previously reported to occur in dung from treated cattle, the treated dung was not appreciably degraded after 340 days in the field. In contrast, untreated dung pats deposited at the same time and place were largely degraded after 80 days in the field [29]. In Australia a field study confirmed the above observations [22]. However, the potential of ivermectin use to affect pasture quality has been the subject of considerable, and ongoing, debate [31, 50, 51], since other experiments were unable to detect any significant change in degradation rate or in the long-term accumulation of dung in the field following treatment with ivermectin [7, 8, 119]. The differences in the results may reflect the diversity of the dung-feeding fauna of the various countries. The high sensitivity of many Diptera to avermectins may explain the negative effects of residues in faeces, since the activity of dung fly larvae plays a major role in disrupting the integrity of dung during the first weeks [98].

In many countries farmers have adopted strategic worm control programs and anthelmintic usage tends to be seasonally synchronous [108]. A model simulating the effects of drug residues on dung beetle populations indicates that controlled-release capsules of ivermectin have the potential to cause substantial declines in beetle numbers, particularly if the treatment coincides with the spring emergence of beetles [110]. In the same way, a model of the effect of deltamethrin on the breeding success of dung beetles in the field suggests that a single pour-on treatment of this drug may reduce beetle activity in the next generation by more than 70% if the time of application coincides with peak beetle emergence in spring. Two or more successive treatments at three weekly intervals had the potential to drive beetle populations towards local extinction unless there is significant immigration from surrounding untreated areas [115]. A similar situation was described in Mexico with a herbicide widely used to control weeds in pastures, which drove local dung beetle populations towards extinction (due to drastic reduction in female fecundity) when the herbicide was applied during the beetle breeding period [77]. Forbes [30] reasoned that, at any one time in the field, only a small proportion of dung pats would contain residues of ivermectin, hence beetles can easily move to an untreated pat. However this does not discount the possibility of sublethal effects due to short-term exposure of ivermectin residues [22]. During the warmer months of the year, beetles move from pat to pat every two to four days, particularly when they are abundant and/or immature [87]. Thus in situations in which the whole herd may be treated, the chance that beetles will contact toxic faeces will be very high.

## 5. INDIRECT EFFECTS OF ANTIPARASITIC USE

Insects which breed exclusively in the dung of herbivores, in which anthelmintics are used, are liable to suffer adverse effects. Common species could suffer local extinction but would be able to recolonise any such area [79]. However rare species may not have this recolonisation potential and therefore could be put at risk by the use of avermectins, and particularly when a slow-release bolus is used. As well as influencing the dung-inhabiting invertebrate fauna, the use of some parasiticides could also indirectly affect some species of vertebrates by depleting the quantity of an important food resource. The effects of such invertebrate food reduction would be expected to be especially severe if it occurs at critical times for the vertebrates, such as during the breeding season or when the young animals have to forage and feed for themselves. This concerns many birds [9, 62, 80, 105], a number of species of bats which feed on *Aphodius* beetles and the yellow dung fly *Scathophaga stercoraria* adults [57, 78, 92], and terrestrial mammals such as hedgehogs, shrews and badgers, which feed on a wide range of invertebrates [79].

## 6. CONCLUSION

This review of available data published in the scientific literature shows that residues of many antiparasitics currently registered for the control of internal and external parasites of cattle and other animals are fairly or highly toxic to egg-laying adults or to developing larvae of many non-target dung-breeding invertebrates. It is very difficult to recognize the importance of delayed reactions to non-lethal doses of antiparasitics. This concerns all anthelmintics, but avermectin is one of the most concerned. The vital question concerns the full extent to which the damage influences pastureland ecology, with often a lack of consideration of long-term consequences for cow pat insects [100]. The second problem concerns cow pat breakdown and the possibility of pasture fouling. The sub-lethal responses of non-target fauna are induced at drug concentrations below those measured several days after a standard absorption of the anthelmintic, but the use of a sustained-released bolus will considerably increase the sub-lethal responses. If the reproductive performance of the surviving adults is impaired, the full consequences will not be apparent until the next generation. Some models predict that even a single treatment has the capacity to cause real reduction in beetle numbers and the effect is greater when there are several successive treatments over a period of weeks [115]. It has been estimated that, in 1991, sufficient avermectins were sold to treat 15% of the world population of 1.3 billion cattle. This is undoubtedly an over-estimate since many cattle are treated more than once in a single season, thus the proportion of cattle not treated with avermectin would be greater than reported [30, 81]. However many farmers have adopted strategic worm control programs and anthelmintic usage tends to be seasonally synchronous, avermectins being used routinely together with other parasiticides. Wardhaugh and Ridsdill-Smith [111] summarised one future challenge: are there really untreated refugia in the modern pastoral ecosystem and, if so, how confident can we be that these are sufficiently extensive in both time and space to adequately compensate for any losses that may occur in treated areas? There are two ways to consider the long-term consequences of the use of parasiticides. Either we try to protect the ecosystem function, i.e. dung degradation, or we try to protect the ecosystem structure, i.e. individual species or populations. If the function is favoured, we have to accept the loss of rare species or large reductions in the populations of dung fauna provided that dung decomposition is unaffected. If our concern is structure, then the challenge will be to protect the majority of dung insect species populations, e.g. to protect 95% of the diversity of dung insects (C. Long, pers. comm).

The part played by anthelmintics in pastureland fouling much depends on the nature of drug administration. Measuring the drug concentration in faeces while studying insect demography would go a long way in helping to understand what is really happening in the various experiments [100]. Most results were obtained after only a several week exposition of pats from treated and untreated animals. Long-term experiments are needed, as a persistent reduction in beetle abundance and species diversity can be observed without immediate and notable influence on dung degradation in the field. Cattle, horses, sheep, swine, to varying degrees are all utilised by humans for economic gain. To date, the detrimental impact upon non-target organisms has been considered acceptable in eradicating parasites because of their economic importance to commercial livestock production. Production will increase when these parasites are suppressed but we remain oblivious to the long-term consequences of this action [97]. Anthelmintics are of considerable value in agriculture, but possibly at an unevaluated cost to the greater environment. The serious challenge is to seek to determine the ecological limits to rural activities, to assess much more critically the inadvertent by-products of controlling parasites and pests, and the long-term consequences of these by-products to our commercial animal production systems. Herd [49] pointed out that, in many parts of the world, irrational parasite control programs tend to be the rule rather than the exception and livestock owners are pressured into damaging over-use of antiparasitic drugs. Sustainable parasite control practices have already been summarised [49]. These practices include the elimination of unnecessary year round treatment, the use of ecologically safe drugs during insect breeding seasons, keeping avermectin-treated animals off the pasture when dung is the most toxic, and selective chemotherapy of animals with high faecal egg counts will provide added safety [50]. These practices could be easily done, even with a one-month excretion of environmental toxic drugs (e.g. subcutaneous injection, pour-on). Conversely, the use of slow-release bolus which deliver avermectins within 4–5 months appears poorly compatible with sustainable pastureland ecology.

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