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Veterinary Medicines

INSECTICIDAL ACTIVITY OF SYNTHETIC PYRETHROIDS, ORGANOPHOSPHATES, INSECT GROWTH REGULATORS, AND OTHER LIVESTOCK PARASITICIDES: AN AUSTRALIAN PERSPECTIVE

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Abstract—The present review is restricted to the collation and evaluation of information describing the excretion profile and ecotoxicity of veterinary medicines developed specifically for the control of either internal or external parasites of livestock. It identifies numerous gaps in our knowledge and highlights our poor understanding of the environmental fate of many of these chemicals, especially those developed for the control of ticks, lice, and/or biting flies. Residues of most anthelmintics are largely harmless to dung-feeding arthropods, but those of many ectoparasiticides, especially the synthetic pyrethroids, are highly toxic to fly larvae and adult dung beetles. Organophosphates, because they are metabolized extensively and eliminated mostly in urine, are considered to be unlikely to have a major impact on the development or survival of dung-dwelling organisms. The present review stresses the need for better information regarding spatial and temporal usage patterns of veterinary parasiticides, and it examines the role of ecotoxicological models for evaluating their impact on populations of dung-dependent arthropods.

Keywords—Parasiticide residues   Feces   Dung fauna

INTRODUCTION

Veterinary parasiticides are scarce and valuable resources that need to be conserved [1], and the same can be said of the dung fauna, which plays a vital role in the processes of dung degradation, nutrient cycling, and pasture hygiene. In recent years, evidence has accumulated suggesting that the development and use of highly potent, broad-spectrum parasiticides, particularly the macrocyclic lactones (MLs), pose a significant threat to the survival of dung-dependent organisms, such as dung beetles and dung-breeding flies [2,3].

The possibility that the increasing use of veterinary parasiticides could lead to a loss of biodiversity and ecosystem function was first envisaged almost 50 years ago [4]. Concern then centered on the evolving practice of using insecticides such as dichlorvos and phenothiazene [5] as feed additives to control livestock parasites that fed or bred in animal feces. Dichlorvos was found to inhibit the survival of dung beetles and to disrupt the processes of dung degradation [5,6], whereas phenothiazene, one of the more popular anthelmintics of the time, was found not only to be harmful to the dung fauna but also to be responsible for a reduction in the clover content of pastures and a measurable decline in nitrification rates [7].

Pest Diptera, such as *Hematobia irritans* (horn fly), *Stomoxys calcitrans* (stable fly), and *Musca autumnalis* (face fly), were the main targets of this early research [8]. However, as observed in numerous studies (see, e.g., [9–11]), animal feces are home to a broad array of arthropods, many of which play a vital role in the processes of dung degradation yet have no adverse effects on the health or comfort of grazing livestock. Because broad-spectrum insecticides do not distinguish between target and nontarget organisms, such developments were seen as the possible forerunner of insect-free dung [12]. Fortunately, the use of oral larvicides presented a number of technical problems and never gained widespread acceptance for treating large grazing animals [8].

The 1970s and 1980s saw the development of a range of new parasiticides, particularly the avermectins, synthetic pyrethroids (SPs), and insect growth regulators. Because of their high potency at low dosage rates and/or their capacity to withstand degradation in the digestive tract [13], these new compounds encouraged the development of novel methods of drug administration (notably ear-tags, injectable formulations, sustained-release devices, and more recently, pour-on preparations). Such complementary advances in drug technology combined to make parasiticide therapy easier, safer, and more effective, and they also offered greater flexibility in determining the period of protection. Lumaret [6] was the first to suspect that this revolution in animal husbandry, especially where it involved the use of systemic ivermectin, had potentially serious consequences for the dung fauna. This was confirmed by Wall and Strong [14], who demonstrated that the combination of sustained-release technology and ivermectin had a major impact on the survival of numerous dung-feeding arthropods. Their conclusion that widespread adoption of this form of parasite control could threaten the sustainability of pastoral ecosystems through a long-term loss of biodiversity sparked a vigorous global debate that continues today. Unfortunately, this debate has been so focused that the environmental impact of parasiticides other than ivermectin has been almost entirely overlooked. Even closely related compounds, such as eprinomectin and doramectin, have aroused scant interest [3], whereas those belonging to other classes of chemicals have been almost entirely ignored.

At present, more than 250 proprietary products, involving about 38 active ingredients, are available for the control of livestock parasites in Australia [15]. These can be divided into three main groups, namely anthelmintics (mainly comprising levamisole, morantel, closantel, and a suite of benzimidazoles),

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ectocides (consisting of organophosphates, SPs, and a group of biological parasiticides; commonly referred to as insect growth regulators), and endectocides (i.e., the MLs). With the exception of some MLs, none of these products provides livestock producers with any indication of the possible impact on nontarget organisms. Such information is largely the preserve of the scientific literature and, thus, is in a form not readily accessible or meaningful to livestock managers. Although recent surveys in Australia indicated widespread awareness that some chemicals have adverse effects on the dung fauna [16], it also was obvious that many producers were frustrated by the lack of objective information regarding the relative safety of different products. Therefore, a need exists for parasitologists and veterinary entomologists to assemble, evaluate, and disseminate to the grazing industry information regarding nontarget effects of veterinary chemicals. The present review is part of that process and relies heavily on material and ideas presented at a recent invitational workshop on veterinary chemicals [17]. It is confined mainly to parasiticides registered for use against either internal or external parasites of cattle, but when appropriate, it provides information about related compounds used in sheep and horses. Chemicals that are active against both types of parasite (i.e., the MLs) have been the subject of several recent reviews [2,3,18] and, accordingly, are not considered here in any detail.

ANTHELMINTICS

Most parasiticides used for the control of internal parasites of livestock are formulated for rapid uptake and elimination. Some of the more commonly used anthelmintics (e.g., albendazole and levamisole) and flukicides (e.g., nitroxynil) are cleared largely in urine and, thus, are unlikely to have any significant effect on the dung fauna (Table 1). This has been confirmed in the case of levamisole [5,19] and albendazole [20], but no information is currently available for the other compounds.

Among those anthelmintics that associate with the particulate phase of digesta and are excreted mainly in feces, only oxfendazole is known to exhibit insecticidal activity (Table 1). In sheep and goats, 65 to 80% of the dose is eliminated in feces, and the remainder is eliminated in urine [21]. Wardhaugh et al. [22] reported residues of this drug to be active against larvae of the bush fly, *M. vetustissima*, but no evidence has been found for any activity against dung beetles or earthworms [23]. McKellar et al. [24] have shown that morantel is eliminated mainly in feces and may persist in the pat for more than 300 d. However, even at high (unspecified) concentrations, the presence of intact morantel had no effect on the development of the yellow dung fly, *Scatophaga stercoraria* [25].

Two compounds of special interest are closantel and clorsulon, both of which are excreted in feces (Table 1). Closantel, a salicylanide compound, is used mainly for the control of internal parasites. Tregoning [26] and Spradbery and Owen [27] have shown that when used in sheep and cattle, the chemical is effective against myiasis-forming dipteran larvae for up to three weeks posttreatment. Closantel is poorly metabolized, and because as much as 80% of the dose may be excreted unchanged in feces, adverse effects on the survival of dung-feeding organisms are clearly a possibility.

Clorsulon is used for fluke control, commonly in association with the ML ivermectin, which is highly active against a range of dung-feeding organisms. In sheep and goats [28], clorsulon is excreted mainly via urine (50–70%), but in cattle, approximately 70% of the dose is eliminated in feces (http://www.emea.eu.int/pdfs/vet/mrls/059099en.pdf). No information is currently available to indicate if clorsulon has insecticidal properties or whether it promotes any synergistic effects when used in combination with ivermectin, but such a possibility merits investigation.

ECTOCIDES

Organophosphates

Early work on several widely used organophosphate compounds, such as dichlorvos, ruelene, and coumaphos, showed evidence of harmful effects on the dung fauna when used as feed additives [5] or in sustained-release boluses [29]. In the case of dichlorvos, residues in horse dung were sufficient to kill adult dung beetles and dipteran larvae for at least 10 d posttreatment. They also were associated with prolonged delays in dung degradation [6]. Comparable information for currently registered organophosphates is lacking, but the available metabolism data indicate that most organophosphate compounds, when applied topically or parenterally, are extensively metabolized and excreted predominantly in urine (Table 1). Therefore, it seems unlikely that organophosphate preparations will have major effects on the dung fauna. Support for this idea comes from the observations of Bianchin et al. [30], who concluded that a spray-on preparation of trichlorfon had a negligible impact on survival of the dung beetle *Onthophagus gazella*. Nevertheless, considering the importance of these compounds, particularly for the control of lice and flystrike in sheep, further work on the more commonly used organophosphates seems desirable.

Synthetic pyrethroids

Some two decades ago, Kunz et al. [31] demonstrated suppression of a population of dung-breeding horn fly, *H. irritans*, via area-wide (960-km^2) treatment of cattle with fenvalerate-impregnated ear-tags. This prompted Schreiber et al. [32] to examine the possibility that such treatment also may result in reduced abundance and diversity of predatory and coprophagous beetles. No evidence for this was found, leading to the conclusion that such chemicals were unlikely to alter significantly the dynamics of the dung fauna. However, more recent studies in Brazil [30,33,34], southern Africa [35,36], Australia [37], and Denmark [38] have shown that the feces of cattle treated topically with a number of different SPs (e.g., cypermethrin, deltamethrin, or cyhalothrin) (Table 1) can be highly toxic to adult dung beetles and/or dung-breeding flies for periods of two weeks or longer posttreatment.

The above-described findings are consistent with the limited excretion data available for SP usage in cattle and other large domestic animals. Although in rats and mice SP residues are eliminated largely in urine, in cattle substantial amounts are excreted in feces—and mostly as intact drug (see, e.g., Croucher et al. [39] for cypermethrin, Ridlen et al. [40] for resmethrin, and Venant et al. [41] for deltamethrin)). In the case of the latter compound, Akhtar et al. [42] found that 36 to 43% of orally administered deltamethrin appeared in feces within 24 h after dosing, with most (72–82%) being present as unchanged drug. However, in cattle treated topically with a pour-on formulation of deltamethrin [41], a much higher proportion of the dose (96–98%) was eliminated in feces, suggesting that the delivery route may be important in determining the excretion route.

Table 1. Elimination route and insecticidal activity of residues of some major veterinary medicines used for the control of internal and external parasites of livestock[a]

Chemical	Main excretion route	Insecticidal activity in feces[b]	Source
Anthelmintics and flukicides			
Levamisole	Urine	No	[86],[c] [5,19][d]
Albendazole	Urine	No	[87],[c] [22][d]
Nitroxynil	Urine	NA	http://www.emea.eu.int/pdfs/vet/mrls/0452928en.pdf[c]
Oxfendazole	Feces	Yes/no	[21],[c] [69,23][d]
Fenbendazole	Feces	No	[88],[c] [6,61][d]
Mebendazole	Feces	No	http://www.emea.eu.int/pdfs/vet/mrls/062599en.pdf,[c] [6][d]
Morantel	Feces	No	[24][cd]
Triclabendazole	Feces	NA	[89][c]
Clorsulon	Feces	NA	http://www.emea.eu.int/pdfs/vet/mrls/059099en.pdf[c]
Closantel	Feces	NA	[90][c]
Diazinon	Urine	NA	http://www.apvma.gov.au/chemrev/diazinon.shtml[c]
Organophosphates			
Chlorfenvinphos	Urine	NA	http://www.apvma.gov.au/chemrev/cfvpchem.shtlm[c]
Propetamphos	Urine[e]	NA	[91][c]
Phosmet	Urine	NA	http://www.fao.org./docrep/W8141/w8141e14.htm[c]
Fenthion	Urine	NA	[92][c]
Famphur	Urine	NA	[93][c]
Trichlorfon	Urine	No	http://www.inchem.org/documents/ehc/ehc/ehc132.htm,[c] [30][d]
Temephos	Urine[e]	NA	http://www.inchem.org/documents/pds/pds/pest8_e.htm[c]
Maldison	Urine	NA	http://www.pmep.cce.cornell.edu/profiles/extoxnet/haloxyfopmethylparathion/malathion-ext.html[c]
Synthetic pyrethroids			
Alpha-cypermethrin	Feces[e]	Yes	http://www.emea.eu.int/pdfs/vet/mrls/080001en.pdf,[c] [34,36,38][d]
Cypermethrin	Feces[e]	Yes	http://www.inchem.org/documents/jmpr/jmpmono/v81pr10.htm,[c] [30,34,35][d]
Deltamethrin	Feces	Yes	http://www.inchem.org/documents/ehc/ehc/ehc97.htm,[c] [41],[c] [30,33,34,37,38][d]
Cyhalothrin	Feces[e]	Yes	http://www.emea.eu.int/pdfs/vet/mrls/069999en.pdf,[c] [30,34][d]
Cyfluthrin	Feces[e]	Yes	[38][d]
Flumethrin	Feces[e]	Yes/no	http://www.inchem.org/documents/jmpr/jmpmono/v96pr07.htm,[c] [30,34,35,38][d]
Fenvalerate	Feces[e]	No	http://www.emea.eu.int/pdfs/vet/mrls/084002en.pdf,[c] [32][d]
Permethrin	Feces[e]	NA	[94][c]
Amines and insect growth regulators			
Amitraz	Urine	NA	[95],[c] http://www.man.ac.uk/umec/extra/factsheets/Amitraz.htm[c]
Diflubenzuron	Feces	Yes	[45],[c] [46,47][d]
Triflumuron	Feces[e]	Yes	[48][d]
Dicyclanil	Feces[e]	NA	http://www.emea.eu.int/pdfs/vet/mrls/057399en.pdf[c]
Cyromazine	Urine	NA	http://www.emea.eu.int/pdfs/vet/mrls/060699en.pdf[c]
Fluazuron	Feces	NA	[49][c]

[a] Modified from Wardbaugh [15].
[b] Yes/no indicates contrary findings on ecotoxicity. NA = no information available.
[c] Source of elimination data.
[d] Source of ecotoxicity data.
[e] The main elimination route is uncertain.

Delivery route also may influence the impact of SPs on the dung fauna [30]. Although their data are few, Bianchin et al. [30] concluded that insecticidal effects associated with pour-on formulations of several SPs were greater than those formulated as sprays, which, in turn, had a greater effect than ear-tags. This conclusion, which reflects the extent to which different preparations are absorbed, is consistent with the observations of Vale et al. [36], who showed that the concentration of deltamethrin in feces voided by cattle treated with a pour-on formulation of deltamethrin was approximately 10-fold higher than that encountered in feces produced by cattle treated with a spray-on preparation.

In a study concerning the ecotoxic effects of deltamethrin, Wardhaugh et al. [37] showed that dung voided by cattle treated with a pour-on formulation of deltamethrin was toxic to adults of two species of scarabaeine dung beetle, *O. binodis* and *Euoniticellus fulvus*, as well as to larvae of the bush fly, *M. vetustissima*, for at least 7 to 14 d after treatment. Deltamethrin was detected in feces as early as day 1 (0.1 ppm) and peaked on day 3 (0.4 ppm). Concentrations remained high (0.09 ppm) on day 7 but fell below the level of detection (0.02 ppm) by day 14. A similar excretion profile was obtained by Vale et al. [36] when dosing with a spot-on preparation of deltamethrin. Using a simple ecotoxicological model, Wardhaugh et al. [37] concluded that a single pour-on treatment of deltamethrin may reduce beetle activity in the next generation by more than 70% if treatment coincided with peak beetle emergence during the spring. Two or more successive treatments at three weekly intervals, which are not uncommon in Australian dairy herds, were shown to have the potential to drive beetle populations toward local extinction. In Queensland, Australia, where ticks and hematophagous flies are endemic, 60% of beef cattle producers rely on SPs for control of the buffalo fly (*Hoematobia irritans exigua*). Synthetic pyrethroids also are used by 37% of producers for tick control [16]. In such environments, SP residues likely have a profound impact on populations of dung-degrading insects.

In South Africa, where cattle may be treated with SPs two or three times per month [43], Kruger et al. [35] used the dung beetle *E. intermedius* to compare the effects of two widely used SPs, namely pour-on formulations of cypermethrin and flumethrin. The toxicity profile of cypermethrin was very similar to that of deltamethrin, with beetle survival being unaffected in feces collected during weeks 2 to 4 posttreatment but virtually inhibited in dung voided during week 1. In contrast, flumethrin was found to be harmless. Although this finding was consistent with the results of previous field studies concerning dung degradation [44], it was contrary to claims by South African graziers that flumethrin treatment was commonly associated with substantial dung beetle mortality. Kruger et al. [35,44] were unable to resolve this discrepancy but suggested overdosing as a possible explanation. However, they also acknowledged that their results were at variance with those of Bianchin et al. [30,34], who found that cattle dosed at the same rate with a similar preparation of flumethrin produced dung that was toxic to adults of *O. gazella* for periods of two to three weeks posttreatment. Studies of other parasiticides often have noted marked variations in toxicity between species (see, e.g., Lumaret and Errouissi [2]), but no records of differences as extreme as those recorded for flumethrin are available. Therefore, other factors seem likely to be involved.

More recent bioassays using the common dung fly, *Neomyia cornicina* [38], have yielded data that strongly support the findings of Kruger et al. [35]. Apart from causing a slight delay in sexual maturation, dung from flumethrin-treated cattle had no detectable effects on juvenile survival or larval growth rates. In contrast, alpha-cypermethrin, deltamethrin, and cyfluthrin all delayed sexual maturation of *N. cornicina* and inhibited larval survival for one to two weeks posttreatment. In addition, larvae feeding in dung collected two to four weeks after treatment were significantly smaller than those developing in the dung of untreated animals. Further dung beetle studies on flumethrin seem to be warranted.

Insect growth regulators

Numerous chemicals act as parasite-control agents by disrupting insect development. However, relatively few of these have been registered for veterinary use, and little is known about their ecotoxicity. The most important are diflubenzuron, triflumuron, fluazuron, cyromazine, and dicyclanil (Table 1). Diflubenzuron, triflumuron, and fluazuron are all chitin esterase inhibitors, but the mode of action of cyromazine and dicyclanil remains uncertain (http://www.dpi.qld.gov.au/sheep/9009.html).

Diflubenzuron is used for the control of lice on sheep and cattle. It is eliminated mainly unchanged in feces [45] and is active against a range of coprophagous Diptera [46]. Fincher [47] found that dung voided by animals treated with a bolus formulation of diflubenzuron inhibited the survival of fly larvae, *H. irritans*, for up to 21 weeks posttreatment and larvae of two species of dung beetle, *O. gazella* and *Sysphus rubrus*, for seven weeks. Diflubenzuron applied as a dust also has been reported to result in the production of dung that is toxic to fly larvae, but no information is currently available regarding its insecticidal activity when used as a pour-on.

Little information is currently available about triflumuron. However, when it was given to cattle as a feed additive, the resultant dung was highly toxic to the larvae of *M. domestica* and *M. autumnalis* [48].

Fluazuron is a systemic, chitin esterase inhibitor used as a pour-on formulation for tick control. It is highly lipophilic and is eliminated mostly as unchanged drug in feces (http://www.vetiran.com/tv1/Subjects/Fluazuron.htm). Studies with an injectable formulation [49] indicated that 95% of the dose was eliminated in feces over a period exceeding 16 weeks posttreatment. Accordingly, a pour-on formulation of fluazuron was expected to result in peak fecal concentrations of 100 ppb some two to four weeks after treatment. Fluazuron was noted to be active against hematophagous Diptera, but no data are currently available in the public domain describing its effects on dung-feeding arthropods. Because fluazuron is widely used in tick control programs in northern Australia, knowledge of its impact on nontarget fauna has been assigned priority status [50].

When used as a feed additive for cattle, cyromazine was found to be active against dung-breeding fly larvae but had negligible effects on dung beetles [51]. However, when given orally to sheep, cyromazine is rapidly absorbed and excreted almost entirely in urine, mostly as parent drug (http://www.emea.eu.int/pdfs/vet/mrls/060699en.pdf). In sheep treated with a topical formulation of cyromazine, most of the dose was retained in the fleece, suggesting that very little of the parasiticide will appear in feces. The situation regarding dicyclanil appears to be similar. When given orally to sheep, dicyclanil is mostly excreted in urine, but when administered topically, which is the recommended method of application, only 2 to 4% of the drug is absorbed through the skin (http://www.emea.eu.int/pdfs/vet/mrls/057399en.pdf).

EARTHWORMS AND VETERINARY CHEMICALS

Despite the fact that earthworms can play a major role in the processes of dung degradation, especially in temperate pastures [52–55], few studies have explored the impact from residues of veterinary parasiticides on earthworms. Apart from some work on fenbendazole [56], most studies have been concerned mainly with the effects of MLs and, therefore, are outside the scope of the present review. However, on the basis of the limited information available, residues of veterinary parasiticides are considered to be unlikely to have any direct impact on earthworm biology [57]. However, the rate of dung removal by earthworms is closely dependent on the previous activity of other dung-feeding arthropods, particularly flies and beetles, which aerate the pat and make it more attractive for earthworm colonization [52,53,58]. Thus, although at present no evidence is available that excreted parasiticides exert a direct effect on the development or survival of earthworms, the fact that that drug residues may inhibit the survival of fly and/or beetle larvae and, hence, disturb the processes of succession [59,60] is a matter that merits further study.

EFFECTS OF PARASITICIDE RESIDUES ON DUNG DISPERSAL AND ARTHROPOD POPULATIONS

The problem of parasiticide residues and dung dispersal has two aspects. The first relates to the immediate impact of chemical residues and their effects on arthropod colonization and activity. Because of the seasonal nature of parasite treatments and the choice factor in the mix of chemicals available to graziers, such effects likely are intermittent in both time and space. Thus, except for drugs that may disrupt the processes of dung degradation for prolonged periods (e.g., the sustained-release bolus of ivermectin [61]), any immediate effects of parasiticide residues on dung dispersal are likely to be rather ephemeral and unlikely to have a major impact on the nutrient economy of pastures [62].

The second, and by far the more important, influence of parasiticide residues is the extent to which their insecticidal activity may induce long-term and/or area-wide changes in the composition and abundance of the dung fauna, leading, in turn, to a chronic problem of dung pollution and a progressive loss in pasture productivity [3]. Unfortunately, this area of research has received little study. In South Africa, Kruger and Scholtz [63–65] monitored insect populations in two 80-ha paddocks over a two-year period following the treatment of cattle with a single annual dose of ivermectin. Although treatment in the first year, which was dry, resulted in measurable decreases in insect abundance and diversity for one to three months post-dosing, similar effects were absent in the second year, which was wet. Kruger and Scholtz [65] considered the differences between years to result mainly from weather, but they acknowledged that such trials needed to be carried out on a much larger scale to be meaningful. However, increasing the size of the treatment area beyond that of a single farm inevitably incorporates greater environmental complexity and a corresponding increase in the problems of data interpretation [66,67].

Because of the high cost and uncertain outcome of field-based evaluations of parasiticide residues, attention is turning increasingly to computer modeling [68]. Although no substitute for field studies, models based on sound ecological knowledge can be powerful tools for examining the likely impact of novel control strategies. They also present a convenient and impartial way of assessing possible outcomes over a range of temporal and spatial scales [66]. Amid growing concerns about the impact of veterinary chemicals in the United Kingdom, the conservation body English Nature has assembled a modeling group to evaluate population responses of dung-dependent invertebrates and associated flow-on effects at different trophic levels in the food chain (Alistair Burn, English Nature, Peterborough, UK, personal communication). Sherratt et al. [66] and Wardhaugh et al. [20,37,69] have already demonstrated the potential value of simple ecotoxicological models and used them for assessing the quantitative impact of single or multiple treatments of antiparasitic drugs on uni- and multivoltine species of scarabaeine dung beetles and/or dung-breeding flies. More recently, in response to environmental concerns about the frequent and widespread use of SPs for control of the tsetse fly (*Glossina* spp.) in southern Africa, Vale and Grant [67] have developed a more complex model that not only allows density-dependent recovery of insect populations but also provides for insect movement into and out of the treated area. These models are not validated, nor do they allow for sublethal effects associated with parasiticide residues, some of which may be just as disruptive as reduced survival (e.g., extended juvenile development or reduced fecundity [70]). Nevertheless, in their present form, these models have identified a number of factors that are considered to be important in determining the variable impact of veterinary drugs (e.g., drug formulation, time and frequency of treatments, proportion of animals treated, etc.). As such, they are useful for identifying knowledge gaps and are valuable for setting research priorities. They also provide an objective way of comparing the potential ecotoxic effects of veterinary chemicals with differing excretion profiles [71]. This latter attribute has obvious applications for regulatory authorities.

CONCLUSIONS AND FUTURE DEVELOPMENTS

Two major conclusions can be drawn from the present review. First, MLs are not the only class of chemical with the potential to adversely affect the development or survival of dung-feeding arthropods. Table 1 shows that most SPs and several insect growth regulators also are excreted in feces at concentrations sufficient to disrupt fly and/or beetle breeding for periods of one to two weeks posttreatment. Under Australian conditions, SPs probably are the more damaging of the two classes, largely because they are used in all sectors of the livestock industry whereas most insect growth regulators are registered for use on sheep only.

The second, and the more important, conclusion is that little or no information is currently available with which to assess the ecotoxic potential of nearly half the antiparasitic drugs presently used by the Australian livestock industry. This is especially evident in the case of organophosphates, but it also is true for many commonly used anthelmintics (Table 1). Such gaps in knowledge make it difficult for livestock producers interested in promoting a healthy dung fauna to adopt a proactive role in pasture and livestock management. Moreover, because the registration of many of these compounds, particularly the organophosphates, predates recent environmental concerns about off-target effects of excreted residues, specific information detailing their impact on the dung fauna probably is unavailable even in the archives of veterinary pharmaceutical companies. Therefore, the challenge for science administrators is to find the resources to conduct the bioassays needed to fill the knowledge gaps in our current database. This process could be simplified if information regarding usage patterns of veterinary parasiticides was available. Such information would allow attention to be focused on those chemicals used most often when beetles are active. However, surprisingly, Australia has no central authority responsible for the collation of such data. A Joint Working Party set up by the Standing Committee on Environmental Protection and the Standing Committee on Agriculture and Resource Management (J. Jeffery and M. Hyman, Draft Report, Standing Committees on Environment Protection and Agriculture and Resource Management, Canberra, Australia, unpublished data) acknowledged this deficiency and identified a number of key policy areas where data regarding the usage of agricultural and veterinary chemicals would be useful. However, the Committee was unable to agree on a number of important issues, mainly relating to collection methods and the spatial and temporal resolution of the proposed surveys. As a consequence, the project was shelved. Meanwhile, the National Association for Crop Protection and Animal Health has begun developing its own database of agricultural and veterinary pesticides [72]. This database is intended to provide information regarding pesticide usage (in both volume and dollar terms) but likely will be some time in the making. Thus, further progress in identifying those drugs liable to have adverse effects on the dung fauna must rely on educated guesses by experts in the field. More importantly, the lack of reliable data regarding chemical usage patterns undoubtedly will impose severe constraints on our ability to explore the benefits of ecotoxicological modeling, which, at present, seems to be the only practical way of gaining an overall insight regarding the environmental impact of veterinary medicines.

In a recent, broad-ranging appraisal of anthelmintic and endectocidal drugs, McKellar [25] concluded that MLs constituted the greatest risk to the survival of dung-breeding arthropods. However, like Roncali [73] and Forbes [74], he argued that insect activity and ML usage patterns often were asynchronous in time and space, thus allowing insect populations to be replenished via migration from untreated areas. In Australia, such a proposal has attracted little support [75], mainly because it relies heavily on the premise that MLs are the sole class of parasiticide with adverse effects on the dung fauna. Given the uncertainties surrounding the organophosphates and the demonstrated insecticidal properties of most SPs as well as some insect growth regulators, this clearly is not the case. Indeed, it may well be that SPs, because of their adulticidal properties, pose a greater risk to the dung fauna than MLs do [30,37]. Moreover, the replenishment scenario begs the question of what constitutes an untreated refuge in modern farming systems, where perhaps as much as 80% of pastoralists may be reliant on the routine use parasiticides (see, e.g., Edwards [16]). Modeling the impact of SP usage on dung insects in Zimbabwe, Vale and Grant [67] concluded that the influence of antiparasitic therapy likely extended well beyond the domain of the treated herd and, to ensure that untreated areas acted as safe havens, these areas needed to be compact blocks with dimensions equivalent to at least 25-fold the distance that an insect might travel in a single day. However, in Australia, the main problem with relying on a process of recolonization from untreated areas is the deficient nature of the arthropod fauna commonly associated with cattle dung. Although more than 300 species of dung beetle are native to Australia [76], only a few (notably *O. australis*, *O. ganulatus*, and *O. ferox*) use bovine dung [77,78]. Most are adapted to woodland habitats and show a strong preference for marsupial dung [79]. Accordingly, the dispersal of cattle dung is almost entirely dependent on the activity of a small number of exotic species of dung beetle. The latter were deliberately introduced into Australia during the second half of the 20th century to encourage rapid dung dispersal and destruction of fly breeding sites [11]. Some 49 species, mostly from Africa and southern Europe, were released over two decades beginning in the mid-1960s, and 25 species are now regarded as established [80]. Some species have spread widely and rapidly, but others have yet to achieve their potential distribution despite several large-scale manual redistribution programs [81,82]. Recent surveys have demonstrated that most grazing habitats in pastoral Australia are home to three or more species of introduced dung beetle [81], with some areas (e.g., southeastern Queensland [82]) supporting as many as 7 to 12 species. However, the interval between introduction and effective establishment (i.e., when beetles are easy to find and play an obvious role in dung degradation) usually is measured in terms of years rather than months [76]. Moreover, their rate of spread often is very slow. As noted by Edwards [82], *Copris elphenor* and *Onitis caffer*, although locally abundant, have spread only some 50 to 70 km from their original release sites during the 20 years since their introduction. Thus, if or when parasiticide treatments severely disrupt beetle breeding, affected populations could take several seasons to recover even when seasonal conditions are persistently favorable for breeding. Accordingly, if Australia is to protect the perceived long-term benefits of its dung beetle program, which include enhanced nutrient cycling, better pasture hygiene, and reductions in the number of pest flies, it is important that we minimize any adverse impacts of veterinary medicines on the dung fauna. To do this, graziers need access to reliable information that enables them to make informed choices about chemical usage. This issue was discussed at some length at the Brisbane workshop on veterinary parasiticides [17] and led to the publication of two information leaflets, one dealing with the strategic use of parasiticides [83] (http://www.agforceqld.org.au) and the other summarizing what is known about off-target effects of many commonly used parasiticides [84]. Initially, the leaflets were aimed solely at livestock producers in tropical areas, but because of widespread interest among graziers in southeastern Australia, a revised set of leaflets has been produced for temperate beetles.

One of the main outcomes of the global debate concerning veterinary parasiticides is that regulatory authorities worldwide are now highly conscious of the need to consider nontarget effects as part of the drug registration process. From a user standpoint, this already has resulted in more informative product labeling and, in the long term, is likely to encourage the development of increasingly pest-specific medicines. The issue of nontarget effects also has drawn attention to the need to develop internationally agreed-on protocols for assessing drug toxicity [85]. This has led to the formation of an international working group (Dung Organism Toxicity Testing Standardization), the main aim of which is to develop standard protocols acceptable to the international community for the registration of veterinary parasiticides. Dung Organism Toxicity Testing Standardization held its first meeting in the United Kingdom in February 2002, and it now includes representatives from research institutions, regulatory authorities, and the veterinary pharmaceutical industry in North America, Africa, Australasia, and most countries in Europe. Dung Organism Toxicity Testing Standardization has formulated detailed protocols for parasiticide testing using specified species of dung-feeding Diptera and Coleoptera. A program of ring testing is about to commence and, if successful, is expected to result in the development of a set of uniform guidelines for drug registration.

Although the above-described initiatives indicate tacit acceptance that parasiticide residues can be harmful to the dung fauna, conclusive evidence that our growing dependence on antiparasitic drugs is likely to lead to a progressive loss of biodiversity or ecosystem function remains elusive. We have good evidence that individual chemicals can have measurable impacts at the herd or flock level, but the extent to which such events combine to influence local, district, or regional populations of dung-degrading arthropods remains highly speculative. Unfortunately, without deliberate governmental intervention to make such studies mandatory and the provision of substantial research funding, it seems unlikely that significant progress will be made in this key area of research in the foreseeable future. In the meantime, the best we can hope for is that livestock producers will heed the warnings of parasitologists and veterinary entomologists to choose, when possible, chemicals with little or no effect on the survival of dung-degrading arthropods, to avoid overdosing, and to treat livestock as infrequently as possible and at those times that are least likely to have a major effect on the processes of dung degradation.

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