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<https://doi.org/10.55457/piahw.005102>

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This publication may be cited as:

McMenamin, C., Miller, L., Cameron, K. E. (2026). Systematic literature review on the ecotoxicity and impact on non-target invertebrate populations of fluralaner used in veterinary administration. *Perspectives in Animal Health and Welfare*, 5(1): 14–28.

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Systematic literature review on the ecotoxicity and impact on non-target invertebrate populations of fluralaner used in veterinary administration

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Senior Editor: Kristina Naden

Article type: Research paper

Abstract

Recent studies have shown that antiparasitic treatments used in companion animal species can impact local ecosystems. With the global rise in feline and canine ownership, there is a corresponding rise in the use of antiparasitic drugs for companion animals to control parasites such as fleas and ticks. The potential detrimental effects on the environment, non-target invertebrates and humans of proactively treating companion animals to combat the effects of zoonotic parasites could be greater than previously predicted. A systematic literature review was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline to identify the extent of research on the environmental transfer and impact of fluralaner, a commonly used parasiticide in veterinary practice. PubMed Central and Google Scholar were searched in September 2024 using terms combining 'fluralaner' with 'ecotoxicity', 'environmental impact' and 'non-target invertebrates'. Studies were included if they addressed fluralaner toxicity to invertebrates, environmental transfer or contamination control measures, and were excluded if focused on human, canine or feline health outcomes, and those not published in English. Of 412 studies that mentioned the target words, 20 studies were included in the final review. These highlighted the persistence of fluralaner in the environment, routes of transmission via veterinary applications and the impact on non-target invertebrates. This review validates the need for further research and provides evidence to support informed decision-making by companion animal guardians regarding antiparasitic product selection to balance veterinary stewardship with environmental consideration.

Keywords

Fluralaner, ecotoxicity, antiparasitic treatment, companion animal, environmental impact

Introduction

Companion animal ownership rates are at a high globally. In Aotearoa / New Zealand there are approximately 4.35 million pets (Companion Animals New Zealand 2024), with a population of 5.36 million people (Stats NZ 2026), while in the United States, dog ownership has increased from 52.8 million owned companion canines in 1996 to 89.7 million in 2024 (Larkin 2024). As pet ownership rises, so too does the use of veterinary parasiticides to protect animals and humans from potential zoonotic parasites such as ticks (*Ixodes ricinus*, *Dermacentor reticulatus* and *D. variabilis*) and sarcoptic mange (*Sarcoptes scabiei* var. *canis*) (Perkins 2020; Perkins & Goulson 2023). In 2023 over 86% of dog owners and 91% of cat owners surveyed in the United Kingdom had administered an ectoparasiticide treatment in the preceding 12 months (Perkins & Goulson 2023). Multiple contamination pathways from treated animals to waterways have now been documented, including the washing of pet bedding and direct entry via the animal's coat during swimming, and transfer to human hands following product application (Diepens et al. 2023; Perkins et al. 2020; Perkins & Goulson 2023; Perkins et al. 2024). These findings raise concerns about the cumulative environmental impact of widespread parasiticide use, particularly given rising global pet ownership rates.

Veterinarians ensure stewardship of antiparasitics used to treat ectoparasites and endoparasites; however, given the availability of parasitic treatments and companion animal populations remaining high and stable, large quantities of veterinary chemicals are being transferred to the environment. The potential impact is difficult to estimate, as veterinarians recommend different treatment plans, some having adopted preventative 'blanket' treatment schedules, while others treat only when an animal (or home) presents with an infestation (Elsheikha 2023). The unnecessary use of antiparasitic treatments in healthy non-burdened companion animals may result in exposure of non-target species to the chemicals found within antiparasitics. Whether or not the clinical benefits of such treatments outweigh their impact on the environment and corresponding non-target organisms warrants critical examination.

Potential environmental impacts of companion animal parasitic treatment contamination include affecting agriculturally important species in Aotearoa such as the honeybee (*Apis mellifera*) (Sheng et al. 2019; Yang et al. 2023). It is our contention that the veterinary industry

should be preparing for more active stewardship and collective caution, such as moving compounds similar to fluralaner to restricted veterinary medicine (RVM), and permitting dispensing from veterinary professionals only, or industry representatives who are able to provide advice on the possible negative impacts this compound has on both humans and the environment. This study examines the laboratory studies and suggests the use of fluralaner to explore the contamination risk involved in its common use to treat parasite burdens in domestic animals.

Fluralaner is a commonly used broad-spectrum antiparasitic used to treat canines, felines and poultry. It is categorised as a broad-spectrum isoxazoline insecticide and acaricide that binds to the chloride channels in nerve and muscles cells, blocking neuronal signals and causing paralysis followed by death of target organisms (MSD n.d.). Isoxazoline compounds, including fluralaner, demonstrate a high degree of selectivity for invertebrate nerve and muscle cells over those of mammals such as humans, dogs and cats (Committee for Medicinal Products for Veterinary Use [CVMP] 2014). Notably, toxicology assessments conducted by the CVMP found that the oral and topical lethal dose required to kill 50% of rats (LD₅₀) exceeded 2000 mg/kg body weight (CVMP 2014). A dose of 25 mg/kg has been shown to effectively treat fleas (*Ctenocephalides felis*) in dogs for up to 12 weeks (Taenzler et al. 2014), while a 40 mg/kg dose is effective in cats (Ranjan et al. 2018). The favourable mammal toxicity profile of fluralaner has resulted in approval by the Ministry for Primary Industries as an unrestricted veterinary medicine, which means that it can be purchased over the counter without the approval of a veterinarian for the treatment of cats and dogs.

Despite being considered 'low risk', fluralaner is classified in the National Library of Medicine (2024) report as a hazardous substance. Specifically, the chemical causes mild skin irritation (H316), is suspected of damaging unborn children (H361d) and is considered very toxic to aquatic life (H410). Fluralaner is assigned a Category 2 hazard classification – as hazardous to the aquatic environment. Fluralaner is widely used as a companion animal antiparasitic treatment under the trade name Bravecto®, and is primarily used to control fleas (*Ctenocephalides felis*) and ticks (*Ixodes ricinus*, *Dermacentor reticulatus* and *Dermacentor variabilis*). It can also be used to treat sarcoptic mange (*Sarcoptes scabiei* var. *canis*), demodicosis caused by *Demodex canis*, and ear mites (*Otodectes cynotis*) in canines and

felines (Burgess et al. 2020; Williams et al. 2014).

However, despite being classified as a Category 2 aquatic hazard, fluralaner has not required Environmental Protection Authority (EPA) approval for companion animal use in Aotearoa. Fluralaner persists in the plasma of treated animals up to 112 days following a single dose (Kilp et al. 2014) and has a considerable half-life of 15 days, resulting in it largely being excreted unchanged (Kilp et al. 2014). Ecotoxicity – the potential for chemicals, physical or biological stressors to harm ecosystems – was identified as an underassessed component during the approval process for Aotearoa agrichemicals in *The EPA's role and performance in assessing hazardous substances: A summary of the current state and performance against international benchmarks* (Loan & Woock 2023). This is an issue the organisation has since committed to address in the near future (Environmental Protection Authority 2025).

Structurally, fluralaner contains two trifluoromethyl functional groups commonly incorporated into pharmaceuticals to stabilise molecular structure (Sani et al. 2007; Novás & Matos 2025; National Library of Medicine 2025). Compounds containing trifluoromethyl can lead to the formulation of trifluoroacetic acid (TFA) within the environment, a substance commonly known as a 'forever chemical'. TFAs have been reported to persist in high concentrations in rivers and seas and are becoming an environmental issue (Arp et al. 2024; Joerss et al. 2024). Further, TFAs do not have a clear degradation route – to break down in the environment – and recent studies have highlighted the risk of TFAs to human health (Arp et al. 2024).

There are currently no restrictions on the use of fluralaner in companion animal species such as cats and dogs. It is considered 'low risk' to humans and animals despite significant hazard ratings in terms of its transmission to the environment and non-target organisms. This literature review identifies existing reports of the transfer of fluralaner to the environment, and studies the potential cumulative environmental effects on non-target invertebrates following its veterinary use.

Method

Database search

In September 2024 a systematic literature search was conducted in line with PRISMA guidelines (Page et al. 2021). Databases PubMed Central and Google Scholar were searched with the following search terms: (fluralaner AND ecotoxicity) AND (environment OR harm OR non-target OR risk) AND (aquatic environments OR terrestrial environments); fluralaner AND (environmental impact OR environmental effects) AND (aquatic environments OR terrestrial habitats); fluralaner AND (bees OR "pollinator health") NOT (mammals OR birds); fluralaner AND "non-target invertebrate organisms" AND (acute toxicity OR chronic toxicity OR sublethal). Studies published between 2000 and 2024 were considered eligible for inclusion, reflecting the period following fluralaner's development and commercialisation, with all available literature retrieved up to September 2024 considered for inclusion. Additional studies were identified from the reference lists of included articles and from the European Public Assessment Reports (EPAR) required for the authorisation of parasiticide products in the European Union.

Screening

No hierarchy of evidence was applied, given the limited volume of literature available on this specific topic; all empirical studies were considered, including clinical trials, experimental studies and case studies, provided they met the inclusion criteria. Any papers found that were not in English, were duplicates or studies that focused on plants, canines, felines or human health, or conditions caused in humans/dogs/cats due to treatment or exposure to fluralaner were not included; however, environmental pathways from canines, felines and humans were included. Further removal occurred following the screening of the abstracts for relevance, such as abstracts that did not discuss the toxicity of fluralaner to invertebrates, the environmental transfer or fate of fluralaner, or control or mitigation measures related to environmental contamination by fluralaner. Papers that were in English, clinical trials, experimental studies and case studies that addressed the toxicity of fluralaner to invertebrates, transfer of fluralaner to the environment, and control measures including strategies to reduce, manage or prevent environmental contamination with fluralaner (e.g., environmental risk management) were included (Figure 1).

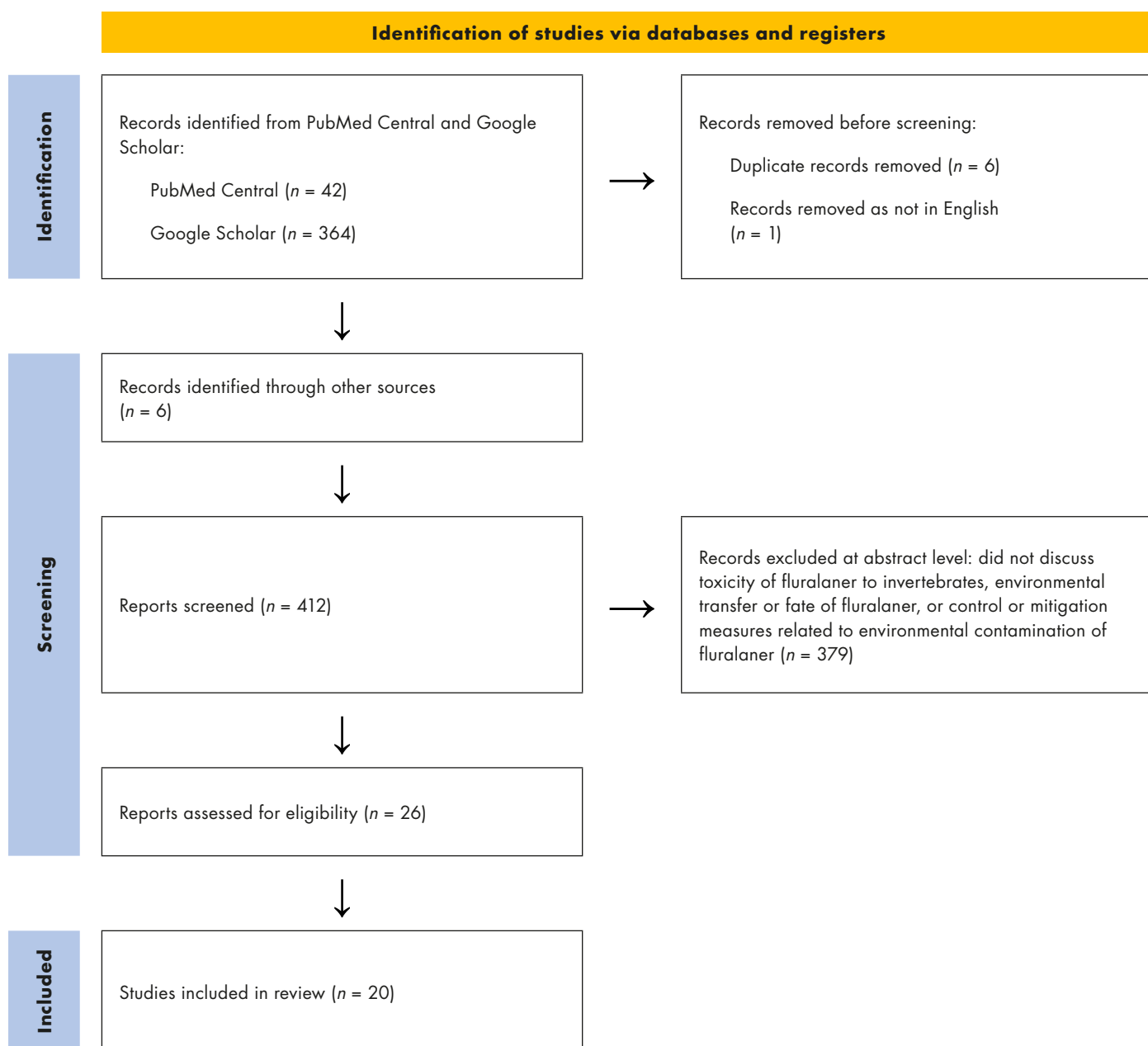


Figure 1. Flow chart detailing the process of identification and screening of papers. Of 412 documents identified in the search, 20 met the criteria for inclusion in the review.

Results and Discussion

This discussion explores three key themes identified from the literature:

1. The ecotoxicity of fluralaner to aquatic and terrestrial environments.
2. The impact on non-target organisms, and lethality and sublethal effects of fluralaner use on non-target invertebrates, including the effects of fluralaner on pollinators.

3. The environmental impact of fluralaner use as pet ownership continues to rise globally, and a call for greater stewardship.

Note: Concentrations discussed have been converted to approximate mg or mg/L values to aid comparison between the amounts of chemicals required to affect different species. These conversions are not precisely accurate in all cases and should only be used as a general guide to understanding.

The environmental impact of fluralaner

Mechanism of action and treatment efficacy

Fluralaner provides long-lasting protection against ectoparasites that act as vectors for a range of zoonotic diseases. These include ticks capable of transmitting *Borrelia* spp., *Babesia* spp. and *Anaplasma phagocytophilum* – pathogens associated with Lyme disease (Petersen et al. 2024) – as well as the cat flea (*Ctenocephalides felis*), which can transmit *Bartonella*, *Mycoplasma* and *Rickettsia* spp., and can serve as an intermediate host for the tapeworm *Dipylidium caninum*. The extended duration of action provided by fluralaner makes it a highly valuable tool in veterinary parasite control.

Transfer of fluralaner to terrestrial and aquatic environments

Environmental risk assessments have raised concerns about the ecological impact of fluralaner. The Committee of Medical Products for Veterinary use (CVMP 2014) reported that approximately 90% of the dose of fluralaner is excreted in faeces unchanged, indicating that faecal excretions from treated animals could retain relatively large quantities of the chemical. Furthermore, the Environmental Protection Authority (2017) product report for Exzolt®, an antiparasitic for poultry, highlights fluralaner's notable persistence in both aquatic and terrestrial ecosystems. In aerobic aquatic environments, fluralaner exhibits moderate persistence with a degradation half-life (DT_{50}) of 40.4 days. In soil, the compound remains highly persistent under both aerobic and anaerobic conditions, with DT_{50} values of 898 and 974 days respectively (Environmental Protection Authority 2017).

While urinary excretion of fluralaner is comparatively low – the CVMP (2014) reported an average of 0.001% (0.0011 to 0.014 mg for doses ranging from 112.5 to 1400 mg) excreted unchanged – even these trace amounts may pose environmental risks. Yang et al. (2023) found that concentrations as low as 90 ng per adult honeybee (*Apis mellifera*) achieved an LD_{50} , demonstrating acute toxicity to non-target pollinators. This finding is supported by Diepens et al. (2023), who detected an average of 1.06 µg/L of fluralaner in canine urine and 1156 ng/g in hair samples, confirming that fluralaner enters the environment through multiple excretion pathways from companion animals.

Environmental persistence and waterway contamination
This finding suggests that fluralaner could be having a

lasting impact on non-target organisms through direct contact with contaminated faeces or contaminate from faeces in soils and waterways (European Medicines Agency n.d.). This highlights potential inadequacies in current guidance provided to companion animal owners. This typically includes advice to avoid bathing or offering swimming opportunities for recently treated animals to mitigate water contamination and minimise environmental release; however, it does not explicitly include management and appropriate disposal of companion animal faeces. Further research is needed to assess the real-world ecological impacts of fluralaner use in companion animals and to evaluate whether additional risk-mitigation measures are warranted.

This idea is supported by Perkins et al. (2020), who found that antiparasitic treatments for companion animals can present as risk factors to waterways. They found that common antiparasitic treatments, imidacloprid and fipronil, were detected in samples from 20 rivers in England. Fipronil was detected in 20 sites (100%) and in 1303 out of 1322 individual samples (98.6 %), while imidacloprid was detected in 19 out of 20 sites (95%) and 873 out of 1325 samples (65.9%). In a later study by Perkins et al. (2024) imidacloprid and fipronil were identified entering waterways after bathing, bed washing and hand washing following the topical treatment of 98 dogs. The largest contaminations were attributed to the bathing of companion animals, ranging from 0.0009 mg to 46.2 mg for imidacloprid and 0.002 to 32.9 mg for fipronil (Perkins et al. 2024). In addition, contamination via hand washing by the owner following treatment to a dog was detected in the washing water for at least 28 days following product application. While fluralaner holds a different mode of action to fipronil and imidacloprid, the risk of contaminants is likely to be similar, considering comparable application and owner interaction with companion animals. This persistence and bioaccumulation potential of compounds such as fluralaner in Aotearoa's unique ecosystems merits urgent investigation, particularly given the country's high proportion of endemic freshwater species.

Impact on non-target organisms

Lethality and sublethal effects of fluralaner to non-target invertebrates

While the majority of literature supports the use of fluralaner in managing pest invertebrates, there has been a limited number of studies that have explored the impacts on non-target invertebrates. This review

identified ten orders of invertebrates (Williams et al. 2015; Asahi et al. 2015; Gassel et al. 2014; Sheng et al. 2017; Burgess et al. 2020; Leviticus et al. 2020; Liu et

al. 2021; Duncan et al. 2023; Yang et al. 2023; Shao et al. 2023) and 23 different species, both target and non-target, that are affected by fluralaner (Table 1).

Table 1. Acute toxicity of fluralaner to non-target invertebrates. Species are grouped by order. Life stage and toxicity measure are reported separately for clarity. LD50 = lethal dose to 50% of the test population; LC50 = lethal concentration to 50% of the test population; LD100 = lethal dose to 100% of the test population. Concentrations have been converted to approximate mg or mg/L values to aid comparison and should be used as a general guide only. Where multiple life stages were reported for the same species (rows 23–24), each is presented as a separate entry.

	Citation	Order	Species	Common name	Time post-application (hours)	Life stage assessed	Toxicity measure	Reported concentration / outcome
1	Duncan et al. (2023)	Diptera	<i>Aedes aegypti</i>	Yellow fever mosquito	24	Adult	>99% mortality	>99% of adult mosquitoes that fed on treated dogs were dead within 24 hours
2	Shao et al. (2023)	Hymenoptera	<i>Solenopsis invicta</i>	Red imported fire ant	24	Adult (worker)	LD50	8.62 mg/kg of adult working ants
3	Yang et al. (2023)	Hymenoptera	<i>Apis mellifera</i>	Honey bee	48	Adult	LD50	0.09 µg per adult bee (0.00009 mg/bee)
4	Yang et al. (2023)	Lepidoptera	<i>Plutella xylostella</i>	Diamondback moth	48	Not specified	LC50	0.02 mg/L
5	Yang et al. (2023)	Lepidoptera	<i>Spodoptera frugiperda</i>	Fall armyworm	48	Not specified	LC50	0.17 mg/L
6	Yang et al. (2023)	Lepidoptera	<i>Spodoptera exigua</i>	Beet armyworm	48	Not specified	LC50	0.12 mg/L
7	Yang et al. (2023)	Lepidoptera	<i>Spodoptera litura</i>	Tobacco cutworm	48	Not specified	LC50	0.19 mg/L
8	Liu et al. (2021)	Coleoptera	<i>Phyllotreta striolata</i>	Striped flea beetle	24	Adult	LC50	0.595 mg/L
9	Liu et al. (2018)	Lepidoptera	<i>Spodoptera litura</i>	Tobacco cutworm	96	1st instar larva	LC50	<0.0625 mg/kg (feeding)
10	Liu et al. (2021)	Coleoptera	<i>Henosepilachna vigintioctopunctata</i>	Spotted potato ladybird	24	Second instar larva	LC50	0.098 mg/L
11	Liu et al. (2021)	Coleoptera	<i>Propylaea japonica</i>	Predatory ladybeetle	24	Third instar larva	LC50	1.177 mg/L
12	Liu et al. (2021)	Thysanoptera	<i>Megalurothrips usitatus</i>	Bean flower thrips	24	Adult female	LC50	0.134 mg/L

13	Burgess et al. (2020)	Diptera	<i>Stomoxys calcitrans</i>	Stable fly	24	Adult	LD50	34.5 ng/fly (0.00000345 mg/fly)
14	Burgess et al. (2020)	Diptera	<i>Haematobia irritans</i>	Horn fly	24	Adult	LD100	4.62 ng/fly (0.0000462 mg/fly)
15	Leviticus et al. (2020)	Trombidiformes	<i>Tetranychus urticae</i>	Red spider mite	24	Adult female	LC50	0.49 mg/L
16	Sheng et al. (2017)	Coleoptera	<i>Tribolium castaneum</i>	Red flour beetle	24	Adult	LD50	107.0 ng/insect (0.000107 mg/insect)
							LC50	214 mg/L
17	Sheng et al. (2017)	Lepidoptera	<i>Chilo suppressalis</i>	Asiatic rice borer	48	Fourth-instar larvae	LC50	3 mg/L
18	Sheng et al. (2017)	Blattodea	<i>Blattella germanica</i>	German cockroach	24	Adult male	LC50	26.9 mg/L
19	Gassel et al. (2014)	Siphonaptera	<i>Ctenocephalides felis</i>	Cat flea	48	Adult	Threshold ≥90% mortality	≥0.01 ppm (ingestion of blood meal)
20	Gassel et al. (2014)	Diptera	<i>Lucilia cuprina</i>	Australian sheep blowfly	48	Larva	Threshold ≥90% mortality	≥1.0 ppm (ingestion of meat diet)
21	Gassel et al. (2014)	Ixodida	<i>Rhipicephalus microplus</i>	Cattle tick	~3 weeks (504 h)	Adult	Threshold ≥90% mortality	≥1.0 ppm (immersion)
22	Gassel et al. (2014)	Ixodida	<i>Ornithodoros moubata</i>	African hut tampan	~3 weeks (504 h)	Nymph	Threshold ≥90% mortality	≥0.0001 ppm (medicated blood diet)
23	Asahi et al. (2015)	Hemiptera	<i>Laodelphax striatellus</i>	Small brown planthopper	Not documented	Not documented	Qualitative	High pest control activity; concentration not provided
24	Williams et al. (2015)	Ixodida	<i>Rhipicephalus sanguineus</i>	Brown dog tick	48	Larva	LC50	0.7 mg/L (contact exposure)
25	Williams et al. (2015)	Ixodida	<i>Rhipicephalus sanguineus</i>	Brown dog tick	48	Nymph	LC50	1.4 mg/L (contact exposure)
26	Williams et al. (2015)	Ixodida	<i>Rhipicephalus sanguineus</i>	Brown dog tick	48	Adult	LC50	278 mg/L (contact exposure)
27	Williams et al. (2015)	Ixodida	<i>Ornithodoros moubata</i>	Sand tampan	48	Nymph	LC50	0.00007 mg/L (feeding exposure)
28	Williams et al. (2015)	Ixodida	<i>Ornithodoros moubata</i>	Sand tampan	48	Nymph	LC50	719.5 mg/L (contact exposure)

Lethality was the main dependent variable in most studies examining the effects of fluralaner. The lethal dose (LD) indicates the amount of substance required to cause death in a given test population. Lethal concentration (LC) is the measure of the concentration of a substance suspended in air or water that will kill a test population. LD50 and LC50, which represent the amount or concentration required to kill 50% of the test population, were the most used levels when assessing toxicity of individual populations in the literature. The research highlights varying levels of sensitivity to fluralaner, with some terrestrial species having high tolerances: in cockroaches, *Blattella germanica* (LC50 26.9 mg/l) (Sheng et al. 2017), red flour beetle, *Tribolium castaneum* (LC50 214 mg/l) (Liu et al. 2021) and striped flea beetle, *Phyllotreta striolata* (LC50 0.595 mg/l) (Sheng et al. 2017).

There is also potential colony-wide impact of fluralaner contamination on red imported fire ants (*Solenopsis invicta*). Research by Xiong et al. (2022) found that transmission of fluralaner among worker ants occurs via contact between treated donor workers and untreated recipients, causing toxic reactions among nestmates. This suggests that fluralaner spread may have a similar impact on species that share behaviours with red imported fire ants, potentially having colony-wide effects with wide longitudinal impacts on similar invertebrate species.

Effects on pollinators

Pollinator species, such as the honeybee, *Apis mellifera* (LD50 0.00009 mg/adult) (Yang et al. 2023), stable fly, *Stomoxys calcitrans* (LD50 0.0000345 mg/fly) (Burgess et al. 2020), and horn fly, *Haematobia irritans* (LD50 0.00462 mg/fly) (Burgess et al. 2020), had significantly lower tolerances to fluralaner. The honeybee (*Apis mellifera*) performs a vital role in pollination and food production (Prata & Martins da Costa 2024). The current decline in pollinator populations, exacerbated by exposure to pesticides, poses a direct threat to agricultural sustainability and animal welfare (Khalifa et al. 2021).

Honeybees are particularly vulnerable to pesticides, their responses often serving as indicators of environmental contamination (Papa et al. 2022). Sheng et al. (2019) found that an LD50 of just 0.13 µg per adult honeybee was sufficient to cause mortality, while Yang et al. (2023) reported an LD50 of 0.09 µg following ingestion of a fluralaner-containing sucrose solution was enough to cause mortality (Table 1). With

pollinator populations already in decline, environmental contamination by veterinary antiparasitic agents risks compounding these losses, with broader consequences for food security and ecosystem integrity (Khalifa et al. 2021; Papa et al. 2022).

Sublethal effects

Sublethal effects of fluralaner also warrant attention, as they can impact invertebrate growth, longevity and reproductive abilities, which contribute to population decline (Xiong et al. 2022; Liu et al. 2018; Sheng et al. 2019; Williams et al. 2014). For example, in tobacco cutworm larvae, low concentrations of fluralaner (LD5 – where only 5% of the population are expected to die) resulted in changes in the development of larvae (Liu et al. 2018). This included reduced body weight, decreased pupation and emergence rates, notched wings in adults, and changes in the transcript levels of genes associated with insect development. These studies highlight fluralaner's potential effect on future populations of invertebrate species (Liu et al. 2018). Additionally, Sheng et al. (2019) found that while fluralaner contamination may not have been lethal, exposed honeybees exhibited impaired neurological function. The authors noted that RDL receptors, which play a broader role in affecting their learning, memory and behaviour, could be affected, raising the possibility that sublethal fluralaner exposure could impair these functions; however, this was not directly tested. In the laboratory, these honeybees showed slowed movement, and should these results translate to wild populations, such concentrations may meaningfully impair honeybee survival; this disruption ultimately threatens the health of other species that depend on a balanced ecosystem for their survival and wellbeing (Khalifa et al. 2021).

Managing environmental risk of fluralaner use in companion animals

Potential for fluralaner overuse

Recent UK studies reveal widespread use of ectoparasitic treatments amongst companion animal owners (Perkins & Goulson 2023). Given the high rates of pet ownership in Aotearoa, with approximately 31% of households owning dogs and 40% owning cats (Companion Animals New Zealand 2024), and high pet ownership globally, there could potentially be thousands of instances of environmental exposure annually. The widespread availability of fluralaner and other antiparasitic

treatments in Aotearoa may lead to overuse or inappropriate application, particularly in healthy animals without confirmed parasite burdens.

The studies by Perkins et al. (2020) and Perkins et al. (2024) demonstrate that companion animal antiparasitic compounds are not effectively degraded before reaching aquatic environments. Their identification of multiple contamination pathways, including bathing, bed washing and hand washing, reveals high emission levels and prolonged environmental shedding that could disrupt aquatic ecosystems. These findings raise concerns about impacts on aquatic invertebrate health and diversity, as well as potentially cascading effects on food webs and habitat stability.

Need for responsible stewardship

These findings advocate for a holistic approach to companion animal health management that balances the clinical benefits of fluralaner against the ecological consequences of contamination. Evidence-based veterinary practice should emphasise integrated pest-management strategies. These include diagnostic confirmation of parasite burdens before initiating treatment, risk-based assessment considering the animal's lifestyle, environment and actual exposure to vectors, and selection of the most appropriate treatment based on both efficacy (ESCCAP 2022) and environmental impact (Perkins et al. 2024). Education of dispensers and purchasers on proper application methods and post-treatment precautions to minimise environmental contamination is also essential.

The effectiveness of veterinarian-led stewardship is contingent on products being purchased through professional channels. In Aotearoa, fluralaner and comparable antiparasitic treatments are classified as unrestricted veterinary medicines, meaning they are freely available for purchase online, in supermarkets and in pet retail stores without veterinary oversight (Ministry for Primary Industries 2016). Where products are purchased outside of a clinical setting, the opportunity for professional guidance regarding appropriate use and environmental precautions is lost. This highlights a critical gap in the current stewardship model and raises broader questions about whether education campaigns targeting the general public, or reclassification of these compounds to restricted veterinary medicine status requiring professional dispensing, may be more effective strategies for reducing environmental harm.

Further research is needed to establish evidence-based guidelines for antiparasitic use in Aotearoa that

account for local ecological sensitivities to develop best practices for minimising environmental contamination during and after treatment, and to assess the long-term ecosystem impacts of veterinary parasiticides in freshwater and terrestrial environments.

Limitations of studies

While there is evidence backing concerns about the unrestricted use of fluralaner in companion animals and its potential impact on the environment, the majority of the included studies were conducted in controlled laboratory settings with small sample sizes; it remains unknown whether findings would translate to real-world conditions where exposure pathways are often indirect and influenced by environmental variability (Xiong et al. 2022; Shao et al. 2023; Liu et al. 2021; Sheng et al. 2019). Further investigation is required in non-laboratory settings with a particular focus on population or colony-wide impacts, as demonstrated by Xiong et al. (2022). Formal quality appraisal was not conducted for included studies, and given the limited volume of published literature specifically addressing fluralaner ecotoxicity, findings should be interpreted with this in mind.

This review's search was limited to PubMed Central and Google Scholar indexes, so it may not have captured literature published in specialist journals or grey-literature sources. The small number of studies meeting inclusion criteria (20 of 412) raises the possibility of publication bias, whereby studies reporting significant toxicity findings may be more likely to have been published than those reporting null results. The exclusion of non-English-language studies may have further limited the catchment of relevant international literature, as translation software was deemed insufficiently reliable for accurate interpretation of technical scientific terminology.

Dosage variability across treated animals of differing sizes means efficacious treatment levels could not be standardised in environmental assessments. Notably, no studies were identified to support the CVMP's claim that fluralaner is excreted largely unchanged in faeces, representing a significant gap in the literature.

Future research

Future research should focus on quantifying the excretion rates of fluralaner, its persistence in various environmental matrices, and its effects on biodiversity, as to date no studies address this specifically.

Such efforts will provide the necessary data to give veterinary researchers the ability to balance the benefits of antiparasitic treatments against the risk of environmental contamination, ensuring the protection of non-target species, including further investigation into their effects on at-risk invertebrates, native species, complex fluctuating agricultural and natural ecosystems, and domestic garden environments.

Conclusion

For many companion animals, particularly those with outdoor access, antiparasitic protection is not merely preventative, but is fundamental to maintaining quality of life and preventing serious illness from flea infestations, tick-borne diseases and sarcoptic mange. However, this systematic literature review highlights the potential environmental risks associated with the transfer and persistence of fluralaner into ecosystems. The documented toxicity to non-target invertebrates, including agriculturally important species such as honeybees, raises important questions about the broader ecological consequences of widespread veterinary parasiticide use. The evidence underscores an urgent need for further research to quantify residual levels of fluralaner in the environment following companion animal treatment; to assess contamination extent in waterways and soils; and to evaluate contamination impacts on ecological systems and biodiversity.

While fluralaner effectively controls parasites and addresses zoonotic concerns, its environmental persistence necessitates careful consideration by veterinarians and animal health-care providers when prescribing treatment. A risk-based approach that balances individual animal welfare with environmental stewardship, prioritising treatment for animals with confirmed parasite burdens or high-risk exposure, may help preserve both companion animal health and ecosystem integrity. Further conversation is warranted regarding whether the use of fluralaner and similar compounds requires additional regulation or professional oversight to safeguard against ecological harm while maintaining sound veterinary care standards.

Abbreviations

mg – milligrams (one thousandth of a gram)
 ug – micrograms (one millionth of a gram)
 ng – nanograms (one billionth of a gram)

LD5 – the dose at which 5% of the test population is expected to die

LD15 – the dose at which 15% of the test population is expected to die

LD50 – the dose at which 50% of the test population is expected to die

LD100 – the dose at which 100% of the test population is expected to die

LC50 – the concentration at which 50% of the test population is expected to die

Declarations

During the preparation of this work the authors used Microsoft Copilot in order to improve readability and clarity of the manuscript. After using this tool/service, the authors reviewed and edited the content as needed and they take full responsibility for the content of the published article.

This research did not receive any grant from funding agencies in the public, commercial or not-for-profit sectors.

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