Aquatic Ecosystems and Environmental Frontiers, Volume 2, Issue 2, June 2024 *ISSN: 3049-186X*
https://doi.org/10.70102/AEEF/V2I2/6

Environmental Persistence of Veterinary Drug Residues in Sediments of Aquaculture-Influenced Water Bodies

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Abstract: Veterinary drugs, mostly antibacterials, are used in aquaculture to prevent and cure diseases, and a substantial amount of drug ingested by fish ends up in the adjacent water body either through uneaten medicated feed or excretion by fish. Sediment underneath and near the farms are the primary sinks of these drug residues, but their persistence is not always comparable among studies. In this review, the persistence of veterinary drug residues in the sediments of water bodies impacted by aquaculture is assessed using scientific literature on this subject available before 2023. Oxotetracycline half-lives found in the reviewed literature vary substantially, from 13 days in well-flushed cages to 144 days in poorly flushed cages. The median of six compiled oxotetracycline half-lives is 62 days, suggesting that the residues persist much longer than the drug treatment period. The residues were detected up to ten months after the last treatment at certain farms. Quinolones, especially oxolinic acid and fluomequine, are strongly adsorbed in sediment and remained unchanged for 180 days in deeper sediments, while florfenicol degraded with a half-life of 4.5 days. Contamination had a spatial range limited to approximately 30 meters from the cages, but quinolone concentrations were as high as 1,166 micrograms per kilogram in a freshwater lake. Resistance genes persisted for years after levels of the drugs could be measured on the farms. Persistence is controlled not just by degradation but by sorption, burial depth, redox environment, temperature, sedimentation, and organic loading. Variation in analysis makes comparison difficult, and freshwater ecosystems are understudied. Multi-depth sediment sampling, standardized half-lives, resistance gene analysis, and ecological risk assessment of legacy contaminants are recommended.

Keywords: Veterinary Drug Residues; Aquaculture Sediments; Oxytetracycline; Quinolones; Half-Life; Antibiotic Resistance; Aquatic Ecosystems.

(Submitted: March 25, 2024; Revised: April 17, 2024; Accepted: May 21, 2024; Published: June 28, 2024)

I. Introduction

Aquaculture is one of the fastest-growing food production sectors, and the growth has seen the widespread application of veterinary medicines as a means of managing diseases caused by bacteria, parasites, and stress reactions. Antibiotics are the most frequently used category of veterinary medicines in aquaculture. They are normally applied using medicated feeds, but the degree of absorption of the doses by fish is not high. Thus, uneaten feed, fecal matter, and urine contain a sizable amount of the applied antibiotics and are released into the aquatic environment, where they find their way to the sediments (Cabello, 2006). In cases where antibiotics are applied in prophylactic measures and in high quantities, biodegradable compounds can persist in the environment and impose selective pressure on microbes for a long time. Environmental behavior of veterinary drugs has been reviewed thoroughly in terrestrial farming, where release of manure and slurry are the major routes of exposure, and up to a significant portion of a single dosage might be eliminated (Sarmah et al., 2006). An aquaculture setting has a distinctive feature: the drug is discharged directly into the aquatic environment, which acts as a natural habitat for organisms of primary interest. Particle-bound drug residues get into the sediments, becoming part of an environmental compartment that features high organic matter content, strong redox gradients, abundant microorganisms, and limited exchange with the overlaying water.

Thus, sediments are the compartment where the long-term impacts of aquaculture chemotherapy are determined. Whereas a residue that disappears from the water column in a matter of hours could still remain in sediments for months, sediment-associated residues can be resuspended, eluted, or taken up by benthic fauna after the chemotherapy process. Persistence influences the exposure time of benthic microbial populations to concentrations at which resistance development is selected and thus influences the time when

a site serves as a source of resistance factors (Cabello, 2006). However, investigations of persistence in sediments are carried out separately in marine cage culture facilities, in freshwater ponds, reservoirs, and laboratory microcosms, use different target analytes (residue concentration versus residual antibacterial activity), and very few attempts to correlate their results have been made.

This paper's objective is to summarize literature up to 2023 on veterinary drug residue persistence in aquaculture-affected sediments. Four questions will be investigated. The first question relates to levels of residues found in the sediments around and underneath the farms. The second one concerns the persistence period of different drug groups and variation in the half-life. The third question is about the scale of residue presence in the environment. The last question is about ecological consequences that these patterns can have for the recipient ecosystems. By analyzing scientific literature on this problem, including results from cage farms, pond systems, mesocosms, and sediment cores, the paper attempts to reveal any patterns, sources of uncertainty and future priorities in monitoring and research.

The rest of this paper is structured as follows: Section 2 discusses the relevant literature about the persistence of antibiotics in aquatic sediments; details the methodology used; Section 3 provides the results and comparative analysis of half-lives of the antibiotics under various environmental conditions; and Section 4 highlights the ecological implications of persistent antibiotics. Section 5 concludes the study.

II. Materials and Methods

2.1 Literature Survey and Selection Criteria

This review is a structured summary of literature rather than a novel field experiment. Literature searches were performed in bibliographic databases and journal websites that considered studies concerning the prevalence, persistence, half-life, or fate of veterinary drugs in sediments related to fish farming. Also, reference sections of relevant papers were hand-searched. Studies were selected if they: (i) reported measurements made on sediments sampled at or near aquaculture sites, or from controlled sediment experiments representative of aquaculture; (ii) contained quantifiable data on concentrations, degradation over time, or spatial extent of occurrence; and (iii) were peer-reviewed studies published prior to 2023. Literature reviews were employed to set the scope for this research but not as a source of primary quantitative data. The ten primary studies, together with two reviews, comprised the dataset, which included marine cage farms in Europe and North America, a farm complex in the Baltic Sea, a salmon-farming area in Chile, a large freshwater lake in China, and urban river sediments (Cabello, 2006; Sarmah et al., 2006).

2.2 Data Extraction and Harmonization

For each paper, data were gathered regarding the study location, drug or drugs investigated, matrix and depth, peak concentrations, half-lives, spatial range of the detection, and any comments made on resistance. Half-lives were collected exactly as reported and did not undergo recalculation, as the time series data used to calculate them were not available. The half-lives and concentrations are given in units of days and micrograms per gram (per kilogram) of sediment, respectively. If there were multiple half-lives reported, such as for multiple cages or sediment depths, each was included and graphed separately.

2.3 Comparability and Limitations of the Dataset

The reported half-lives were not directly comparable to one another as some of the studies measured chemical concentration in the parent substance, some of the studies measured remaining antibiotic activity, and each of these studies had different depths of sampling, sediment types, temperatures, rates of sedimentation and organic matter loading. Microcosm experiments conducted in the laboratory lack the physical processes of burial, resuspension, and advection that occur in the natural environment. Consequently, consider the half-lives to be approximations of an order of magnitude and compare the trends

common to these half-lives rather than rank the individual studies. Qualitative data on resistance gene persistence were collated narratively and were not combined with half-lives in any mathematical way.

III. Results

3.1 Concentrations Recorded in Aquaculture Sediments

High sediment concentrations of oxytetracycline occurred after medicated feed was applied as treatment. In a Galway Bay salmon farm, maximum concentrations in the top 2 cm of sediment under cage blocks were 9.9 ± 2.9 and 10.9 ± 6.5 micrograms per gram for two separate treatments (Suga et al., 2013). In five Nordic fish farms, oxytetracycline ranged from 0.8 to 6.3 micrograms per gram in sediments below the treated pen, and oxolinic acid ranged from 0.05 to 0.2 micrograms per gram in sediments and was detectable only for about five days following treatment (Björklund et al., 1991). In another study carried out on three North American farm sites and microcosms, oxytetracycline was found under cages proportional to the quantity of the antibiotic applied, and there were no detections below a farm using small amounts of the drug (Capone et al., 1996). Therefore, the highest sediment concentrations occur in intensive treatment conditions, and the lowest ones occur in minimal treatment conditions.

In the freshwater system contaminated with aquaculture effluents and other sources, sediment concentrations are relatively low but widespread. In Baiyangdian Lake, North China, quinolones accounted for the majority of antibiotics in sediments, having concentrations of 65.5 to 1,166 micrograms per kilogram, whereas sulfonamides accounted for most of the antibiotics, while the sulphonamides were the predominant pollutants in the water column, ranging from 0.86 to 1,563 nanograms per liter (Li et al., 2012). This comparison demonstrates the importance of sediment sampling since the same class which was negligible in water could be dominating the sediment matrix due to sorption properties.

3.2 Persistence and Half-Lives

Table 1 shows the main results obtained from ten primary studies. Figure 1 depicts the sediment half-lives found in the primary literature sources. Oxytetracycline half-lives in the sediments of marine cages varied by an order of magnitude. For two cage blocks at a salmon farm, the concentration decreased exponentially with half-lives of 16 and 13 days Suga et al., (2013). At a separate salmon farm, 18 months of sampling after a ten-day treatment resulted in half-lives of 125, 144, and 87 days under three cages, where most of the oxytetracycline disappeared in the initial weeks, but the rest of the drug stayed longer (Cabello et al., 2016). Microcosms were used to determine the oxytetracycline half-lives in the laboratory setting with the farm sediment, and 1/4 to 1/2 of oxytetracycline was left after 60 days, whereas the half-life for the only exponential case was 36 days Capone et al., (1996).

Data collected in the field from the same research also showed that the drug could persist for even longer periods. The presence of oxytetracycline was detected in both surface and subsurface soil sediment before a new application was done, showing that the drug could survive for at least the last ten month (Capone et al., 1996). From the two sets of findings, it can be seen that a period of fast disappearance followed by a slow one characterizes the process.

Table 1: Summary of Sediment Persistence Evidence from the Primary Studies Reviewed

Ref.	Setting	Compound(s)	Key sediment finding
Capone et al., (1996)	Three US Marine Farms; Microcosms	Oxytetracycline; Sulfadimethoxine, Ormetoprim	Residues to 30 m from Cages, Absent at 100 m; 36-day half-life in One Microcosm; 25–50% Remained at 60 Days; Sulfonamide/Ormetoprim Short-Lived
Suga et al., (2013)	Irish Marine Salmon Farm	Oxytetracycline	Peak 9.9 and 10.9 µg/g (top 2 cm); Half-Lives 16 and 13 Days; Detected to 8 cm Depth
Cabello et al., (2016)	Fish Farm Sediment, 18-Month Study	Oxytetracycline	Half-Lives 125, 144 and 87 Days Under Three Cages; Resistant Fraction fell to ~20% after 72 days
(Chen et al.,2017)	Seabed Boxes, 180–230 Days	OTC, Oxolinic Acid, Flumequine, Sarafloxacin, Florfenicol, Sulfadiazine, Trimethoprim	Quinolones and OTC Retained Initial Levels at Depth after 180 Days; Florfenicol Half-Life 4.5 days; Sulfadiazine/trimethoprim ~90 Days at 6–7 cm.
Björklund et al., (1991)	Five Nordic fish Farms	Oxytetracycline; Oxolinic Acid	OTC 0.8–6.3 µg/g under Pens; Oxolinic Acid 0.05–0.2 µg/g for 5 days, Faster Loss of Activity
Leal et al., (2019)	Artificial Marine Sediment Tanks	OTC, Oxolinic Acid, Flumequine	~One Third Lost in 20 Days, Further ~25% in Next 165 Days; Resistance Rose within Days
Li et al., (2012)	Baiyangdian Lake, China (Freshwater)	22 antibiotics (Quinolones Dominant)	Quinolones 65.5–1,166 µg/kg in Sediments; Sulfonamides Dominant in Water
Tamtam et al., (2011)	Seine River sediment Core	Quinolones, Sulfonamide	Residues to >80 cm Depth (deposits from early 1960s); Persistence up to 30–40 years
Tamminen et al., (2011)	Four Baltic Sea Farms	Tetracycline Resistance Genes	Genes Persisted Without Therapeutic Drug Levels; One Farm Unmedicated for Six Years; None at 200 m
Buschmann et al., (2012)	Chilean Salmon Farm Area	OTC, Oxolinic Acid, Florfenicol, Flumequine	Resistant Fractions Higher at Farm than Control (8 km); only Flumequine Traces Detected

Note: OTC = oxytetracycline. Values are reproduced as reported by the original authors; half-lives were not recalculated.

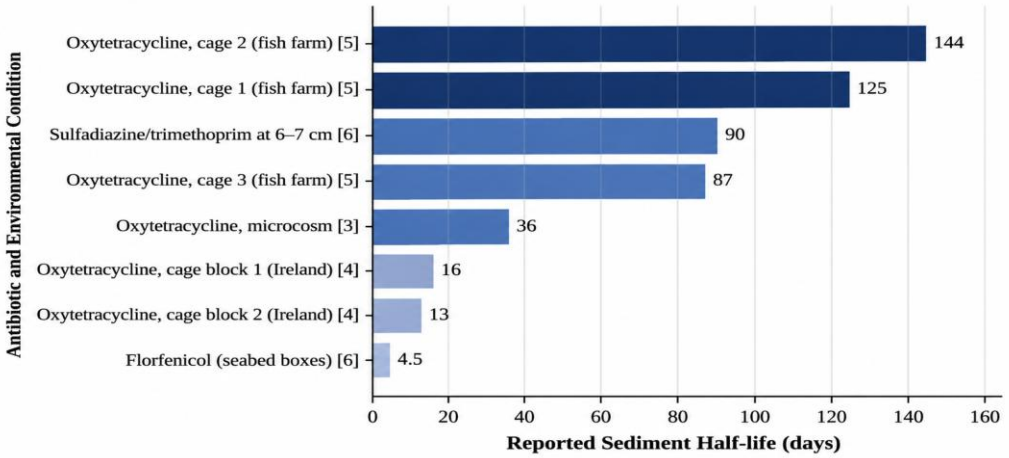


Figure 1: Comparison of Reported Antibiotic Half-Lives in Sediments under Different Environmental Conditions

3.3 Differences among Drug Classes

Persistence of different drugs varied significantly. In an experiment in sea bottom sediments that lasted 180 to 230 days, oxytetracycline and the quinolones oxolinic acid, flumequine, and sarafloxacin showed a high level of persistence: the concentration of those antibiotics in deep sediment layers was retained after 180 days, while residues in the top layer were depurated more rapidly, and the authors ascribed this effect primarily to the processes of leaching and redistribution rather than degradation. It is noteworthy that the quinolones were shown to be adsorbed by the sediments. On the contrary, florfenicol showed a rapid degradation with a half-life of 4.5 days, and its metabolite florfenicol amine appeared in the sediments. Sulfadiazine and trimethoprim were shown to be less persistent than the quinolones, with an estimated half-life in the deepest sediment layer (6 to 7 cm) of about 90 days.

In the laboratory experiment using artificial marine sediment, the same general trend was observed, with about one third of the antibiotic compounds being removed from the sediments during the first 20 days and a further quarter of them being depurated during the next 165 days Leal et al., (2019). However, for the field experiment in the Nordic countries, the oxolinic acid displayed a quicker loss of antibacterial properties than the oxytetracycline, which was detected as persistent under the pens (Björklund et al., 1991). The inconsistency of the data obtained about the persistence of oxolinic acid by chemical and biological methods is due to the methodology used, which will be explained in section 4.1. Finally, the combination of the sulfadimethoxine and ormetoprim, which are components of the potentiated sulfonamide drug, seemed to have an extremely quick disappearance in the marine sediments in contrast to the 90 days half-life of the sulfadiazine and trimethoprim at depth.

3.4 Spatial Extent of Contamination

The size of the residue footprints was usually small. In the Galway Bay farm, residues of oxytetracycline near the end of therapy were identified in an area no more than two times the area occupied by the cages, and were found only in the region expected to be under pelleted feed but not in the region expected to have been under feces alone (Suga et al., 2013). Residues were found up to 8 cm deep nineteen days after therapy; however, concentration decreased at all depths fourteen days after that Suga et al., (2013). In North American farms, residues were detectable underneath cages and within thirty meters but not at one hundred meters from.These data show that deposition of uneaten pellets of the feed was the major factor determining the location of residues.

3.5 Resistance and Ecological Indicators

Biological effects have been associated with the persistence of certain antibiotics. The ratio of oxytetracycline-resistant bacteria in sediments below three cages after 10 days of oxytetracycline therapy was very high initially, decreased to 20% at 72 days, and stabilized at 10-50% Cabello et al., (2016). The antibiotic drugs such as oxytetracycline, oxolinic acid, and flumequine caused bacterial resistance in experimental tanks within days; oxytetracycline caused more resistance than other drugs for a longer time, the number of bacteria decreased to 50-67% of control levels in two days after drug treatment and sulfate reduction to less than 10% of control in seven days, and recovered by day 70 Leal et al., (2019). Sediments 20 m away from a salmon farming facility in Chile contained significantly higher bacterial numbers and fraction of resistance compared to control sites that were 8 km away from the farming site although trace amount of flumequine was detected (Buschmann et al., 2012).

Most compelling examples of persistence in legacies are provided by the Baltic Sea. Tetracycline resistance genes were present in higher numbers compared with control samples collected at pristine sites and at the farm locations during most of the sampling periods, even though none of the farms applied tetracyclines at the time of sampling, one of them stopped using any antibiotics six years before sampling, and none of the samples had therapeutically relevant concentrations of these antibiotics; no genes were found at 200 m distance from the farms (Tamminen et al., 2011). Residues of the substance can persist much longer in certain environments. Quinolone and sulfonamide residues have been detected in a dated

sediment core from the Seine River to a depth of 80 cm, corresponding to the deposits from the early 1960s, which indicates that such substances can persist in sediments for 30-40 years (Tamtam et al., 2011). While this core has been taken from an urban river rather than from a fish farm, it shows the possibility of long-term persistence of highly sorbing antibacterial classes of compounds.

3.6 Synthesis Across Studies

The average of six values obtained from the literature on oxytetracycline's half-life in marine sediments is 13, 16, 36, 87, 125 and 144 days, yielding a median of about 62 days and an arithmetic average of about 70 days (Suga et al., 2013; Cabello et al., 2016). The range is large, but even the smallest values still show that any residue that survived a ten-day treatment will be detectable for several weeks further on; since after five half-lives, which is two or three months in the range of 13 to 16 days, 3% of the original quantity will have survived. This category does not apply to compounds like florfenicol that have a half-life of days; such substances belong to a regime where the sediment accumulation is temporary, and the important aspect is the multiple applications. On the other hand, quinolones belong to the opposite end of the scale and have no observable decrease after six months in the deep layers (Leal et al., 2019).

Three patterns remain constant. One is that persistence depends on the nature of the compound. Second is that persistence varies with depth; deeper depths have higher persistence than surface depths. Third is that persistence is context-based; compounds with identical properties have half-life differences of more than ten times at different sites (Suga et al., 2013; Cabello et al., 2016). This implies that the persistence values of any single compound are site- and method-dependent.

IV. Discussion

4.1 Controls on Persistence

Persistence of quinolones in sediments from aquaculture cannot be linked to only one mechanism. Three categories of control mechanisms seem to operate. First is the physicochemical characteristics of the compound itself. Quinolones bind to sediments, and the high binding affinity of fluoroquinolones to sediments has been documented not only in aquaculture but also in river ecosystems where sediments were found to be an important sink (Li et al., 2012). Tetracyclines are known to form complexes with divalent ions, and the persistence of oxytetracycline in marine sediments while being inactive in some studies is likely due to binding that lowers its bioavailability but not the concentration of the compound. This is a key factor to bear in mind when interpreting results since a chemical test will detect a residue even though it is biologically inactive, while an activity assay will detect a loss of the compound that remains there.

The second category is the physical environment at the farm. Half-lives of 13 and 16 days in a well-flushed setting compare with 87 to 144 days in a 18-month-long study, and reasons for slower degradation might be burial under new material, poor water exchange and heavy organic burden (Suga et al., 2013; Cabello et al., 2016). The observation that the persistence was higher at greater depths than on the surface is another support of the idea that physical movement is responsible for the reduction observed in the top layer, rather than degradation (Chen et al.,2017). Thus, the decline in the concentration on the surface does not necessarily mean the reduction in the amount of drug in the system, since leaching, resuspension and burial change its location.

The third category is the biological and chemical transformation of drugs, and it is highly compound-dependent. In particular, florfenicol was transformed to a metabolite and degraded within a few days, and preliminary data show that sulfadimethoxine and ormetoprim were short-lived on the other hand, oxytetracycline and quinolones persisted for several months (Leal et al., 2019). It is probable that temperature, light and oxygen affect those rates, but they are not always reported together with half-lives.

4.2 Ecological Implications for Aquatic Ecosystems

Ecological importance of sediment persistence is evident in the prolonged exposure of the benthic organisms compared to pelagic organisms. Antibacterials affect processes in which microorganisms are involved in the functioning of sediments. The inhibition of sulfate reduction upon antibacterial addition proves that biogeochemical processes in sediments can be affected; however, in the case of the experiment conducted in a tank, this effect was only temporary (Leal et al., 2019). Changes in the bacterial population of sediments due to high prophylactic use of antibiotics in aquaculture were discovered. In case of persistence, these changes will occur repeatedly in every cycle. Persistence of resistance determinants constitutes another, independent ecological issue. It has been found in the Baltic Sea that resistance genes could survive for a number of years after the selective pressure ceases to exist (Tamminen et al., 2011). Similarly, the case of the Chilean sea demonstrates high levels of resistance genes even in sediments where the parent compound is detected at a negligible concentration (Buschmann et al., 2012). Thus, resistance is a better predictor of aquaculture impacts than the presence of chemicals. The global assessment of veterinary antibiotics has shown that the combination of pathways, fate and effects must be considered (Sarmah et al., 2006). This approach should also be used when assessing aquaculture impacts.

Another issue related to risk assessments of non-microbial organisms has been found in the Baiyangdian Lake: a risk assessment of antibiotics in surface water has revealed that algae and aquatic plants could be at risk of antibiotics whereas animals would not be Li et al., (2012). This conclusion has been made on the basis of surface water concentrations and does not account for the risk to the organisms that live in the sediments. However, sediment concentrations are several orders of magnitude higher than water concentrations.

4.3 Freshwater Systems and the Geographic Gap

The most well-defined half-lives are found in temperate sea-salmon farms, whereas the freshwater and tropical environments, where the majority of the world's aquaculture production takes place, are only characterized by occurrence data and not persistence experiments (Li et al., 2012). There are various differences between freshwater ponds and reservoirs and marine cages, which could influence persistence, including the lack of cationic seawater, lower rates of water exchange, higher temperatures, and sediments being occasionally disturbed by harvesting and pond management. It would be unreasonable to extrapolate the half-life of marine environments to these habitats, and this is the most critical geographic knowledge gap highlighted by this study.

4.4 Implications for Monitoring and Management

Recommendations to be implemented from the findings are many and include: monitoring programs should incorporate the sediments at more than one level as they might give an underestimate of the burden and overestimate recovery. The half-lives should always be documented with its analytical basis whether chemical or activity based, the sediment level, temperature, and organic content for easy comparison in different studies. The third recommendation is the simultaneous monitoring of resistance determinants together with residue levels as they persist even when chemicals cannot be detected (Tamminen et al., 2011; Buschmann et al., 2012). This is because the area covered by detectable residues is small and related to feed deposition, hence selecting the site in such a way as to favor flushing of the bed and the practice of minimizing waste during feeding practices. The other recommendation is the reduction in the prophylactic use of antibiotics as this leads to increase in drug release and exposure.

Assessments of recovery of the site are necessary because a fallowing period estimated on the dissipation of water column would be inadequate for those compounds that persist for more than six months in the sediment.

4.5 Research Priorities

A number of research areas become apparent based on the findings described above. For instance, studies where degradation is separated from leaching, burial and resuspension are needed, such as using mass balance measurements combined with finely stratified sediments in a controlled study. In freshwater ponds, reservoirs and aquaculture systems, measurements of persistence need to be done rather than just estimating persistence indirectly by the means of occurrence studies (Li et al., 2012). Simultaneous analysis of chemical concentrations, residual antibacterial activities and resistance genes from the same locations and sampling times can provide more information to address the discrepancies outlined above. Finally, long-term monitoring of sites prior to, during and after treatment, especially the ones that stopped using antibiotics, will give an idea about recovery times as well as existence of sediment core records similar to the one from the Seine river (Tamtam et al., 2011).

4.6 Limitations

This synthesis, however, has some weaknesses which should be considered. First of all, this synthesis is based on a small number of papers, most of which were carried out in marine cage farms in the period of early 1990's till 2012 and methods of analysis and farming practices have changed since then. Half-lives were directly extracted from the original studies without re-calculation and vary depending on the compartment in which they were measured. Some studies refer to the sites which are impacted by other substances and the core of Seine is not an aquaculture site. Therefore, the parameters presented above can be used just as a range of persistence but not as parameters for site-specific models. Nevertheless, the similarity of patterns which have been observed in independent studies provides confidence in the conclusions.

V. Conclusions

The residues of veterinary drugs in the sediments of aquatic environments influenced by aquaculture have different half-lives from days up to years, and according to the reviewed literature, it can be seen that their persistence depends very much on the type of chemical and also the depth and conditions of deposition in the sediment layer. The half-life of oxytetracycline was between 13 and 144 days; quinolones maintained almost constant concentrations after 180 days in deeper sediment layers; and florfenicol residues disappeared after several days. The residues of drugs were spatially distributed only at the footprint of cages and their neighborhood, however, they had much longer legacy due to the persistence of resistance genes, which survived years after the end of antibacterial treatments, and also the existence of long-persistent compounds in the decadal records of sediments. Sediment sampling at various depths, transparent half-life reporting with analysis basis, and evaluation of the effect of resistance determinants along with chemical concentrations should thus be prioritised by managers. Farm management that reduces wastage of feeds, dosage based on requirement, and choosing suitable locations with enough flushing facilities will ensure that less drugs are flushed into the bed and lesser time is required for its recovery. Priority areas in research would be fresh water ponds and reservoirs, tropical regions, where there is scanty evidence, study that distinguishes degradation from burial and leaching processes, and effect on ecosystem functions. Until such evidences become available, precautionary use of antibacterial agents, backed up by sediment sampling and post-treatment recovery assessment, would be the most prudent course of action for aquatic environments, fisheries, and populations under influence of aquaculture.

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