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# Evaluating the Environmental and Hygienic Impacts of Veterinary Pharmaceuticals: Investigating Risks and Solutions (Article Review)

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## A B S T R A C T

The veterinary pharmaceutical residues have generated critical ecological and human health risks. including antimicrobial, antiparasitic, nonsteroidal anti-inflammatory drugs, these residues can survive in the environment for decades, veterinary medicines specially the antibiotic considered the primary source for bacterial resistance in humans according to the World Health Organization (WHO) short term health associated effect lead to human allergenicity and toxicity while the long term including sever health issues like disruption of intestinal microflora ,carcinogenicity and teratogenicity.An extensive search related to environmental distribution of veterinary pharmaceuticals was performed through researches online databases like (Google scholar, ScienceDirect, Web of Science, and PubMed), then papers collected, analyzed, and explained.The active drugs and their metabolites have contributed globally to aquatics and land contamination. While knowledge is growing, large information gaps remain on their effects. The impacts of these chemicals in the environment are still largely unknown. This review shows a clear need to extensively track not just presence of veterinary compounds in different areas worldwide, but primary sources as well. Identifying sources is key to shaping regulatory monitoring, as it addressing current problems and preventing future issues



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## Introduction

The distribution of various types of veterinary pharmaceuticals has led to serious environmental and public health concerns, particularly in the food products derived from animals. Over the past five years, there has been an increase in the usage of veterinary medicinal products and a corresponding rise in the quantities of these substances entering the environment [1][2]. Veterinary drugs are classified as therapeutic, prophylactic, growth promoter, and functional modulator drugs, including antimicrobial, antiparasitic, nonsteroidal anti-inflammatory drugs, sedatives, corticosteroids, and beta-agonists [3]. According to the European Federation of Animal Health, approximately one-third of the veterinary pharmaceuticals used in poultry and pig farms consist of antibiotics [4]. Pharmaceutical residues from veterinary drugs can be transmitted through animal-sourced food products, animal excretions, and farm utilities into agricultural soil, surface water, groundwater, aquaculture systems, and rivers. Despite associated health risks and their toxic effects on human consumers [5], these residues can persist in the environment for decades, veterinary medicines constitute the primary source of antibiotic resistance in humans according to the World Health Organization (WHO) [6][7].short term health associated effect of drug exposure lead to human allergenicity and toxicity while the long term including sever health issues like disruption of intestinal microflora ,carcinogenicity and teratogenicity [7]. Antibiotic exposure Eliminate nitrogen producing bacteria in the soil, inhibit weeds and crops growth and bioaccumulation, veterinary drug persistence, transformation and availability determined by its reactive characteristics with environmental elements and biodegradability, The process for treating and removing these chemicals is extremely complex [8]. Therefore, the current review aims to highlight the effects of veterinary medicines on human health as consumers of animal products and its impact on the biological and environmental resources as well as, to review the risks of these chemical compounds and the global programs to control its exposure.

### Environmental Impacts of Veterinary Pharmaceuticals

It has been widely recognized by researchers and health specialists that drug pollution is a serious issue that requires immediate and crucial solutions. It is essential to address this problem for enhancing living conditions in a healthy environment, preventing the deterioration of ecosystems, and to prevent the distribution of drug-resistant diseases [5]. The veterinary drugs are often excreted through the urine, feces, and body secretions of grazing animals, directly into pastures, water sources, and farming areas. Additionally, they can enter the environment through the process of fertilizing with manure from intensively medicated animals [2][9][10]. The release of expired animal drugs to water sources, aquaculture, agricultural lands, or through the burial of contaminated carcasses of chronically diseased animals poses significant risks of contaminating groundwater, soil, and the surrounding ecosystems. Moreover, the biological disposal of poultry field wastes, as well as targeted food products from animals with a history of long-term medication, can result in the absorption of these chemicals by the soil or their flow into surface water such as lakes, rivers, lagoons, tanks, etc., and may also reach groundwater reservoirs, agricultural lands, and forests [9][11].

### Contamination of Water resources

- **Surface water**

Diverse veterinary antibiotics were detected in waste water Treatment Plants globally associated with significant human health implications , [12] ,referred that groups of waste water Treatment stations in Canada were contaminated with veterinary purposed sulphamethazine, with concentrations reached up to 3.278 µg/L ,water drained from animal raising farms with concentrating feeding programs ,similar results observed by [13], in the lagoons at different areas close to the cattle and swine facilities in USA ,the water samples examined revealed presence of sulfamerazine, erythromycin, sulfamethazine, tiamulin, monensin, , sulfathiazole and Lincomycin, the authors conclude that groundwater underlying livestock waste water impound with drugs contamination.[14] , also reported the impact of veterinary drug pollution in surface water and pristine area in mountain river (Poland), water samples showed that antibiotics was the higher among other types of drugs including erythromycin (0.89 ng/L), vancomycin (2.99 ng/L), oxytetracycline (0.27 ng/L), sulfamethoxazole (0.20 ng/L), clindamycin (0.36 ng/L), and trimethoprim (0.29 ng/L). Lim et al [8], during examination of water sample from 11 wastewater Treatment Plants, detected analgesics and antibiotics in high concentrations including acetylsalicylic acid, chlortetracycline, oxytetracycline and acid , sulfamethoxazole, erythromycin , and trimethoprim , correlated the amount of contamination with the annual manufacturing of each antibiotic during the year .[15] reported in their study that water treatment stations in Korea were contaminated with veterinary oriented antihelminth drugs like albendazole with doses reached from 3.85-241 ug/L with albendazole metabolites like amino albendazole ,hydroxyfenbendazole and salfon fenbendazole , and suggest that source of these drugs come from livestock farms in the neighboring areas or come through the sewage water.[16] demonstrate the level of oxytetracycline in the water at drainage basin in Japan that reached between 2ng/L to 63 ug/L ,the author suggested that intense usage of this antibiotic in the farms of cattle ,chickens, and swine is the main sourse of contamination particularly, at the winter season where drug used as prophylactic against the respiratory diseases and diarrhea.[17] mentioned that antibiotics concertation in Naerincheon river varied with seasons and noted that sulfonamides and tetracyclines were higher in dry season compared with rainy season and attributed this to the effect of rain in the dilution of drugs concentration and the lower temperature during this season in slowing of biodegradability. [13] found that irrigation area ,and drainage water from dairy cow facilities in many Australian sites were contaminated with penicillin ,oxytetracycline and sulfonamide with concentation reached to 321,109,432 ng/L respectively . and connect these highly pollution with dairy activities and treatment of foot rot (table1, table 2).

- **Groundwater contamination**

The underground water provide a great dependable source of drinking water to humans and animals on our plant, the pollution in this sources of water with chemical substances descended from veterinary pharmaceuticals can be a harmful for public health and restrict animal production process, according to [18] , group of groundwater bodies were investigated in Spain ,Catalonia had a high concentration of sulfonamides formulated drugs reached 3460 ng/L ,represented 20% of the whole chemical drugs contamination in the area .[18] referred that the source of contamination of the water result from fertilizing of organic manure fertilizer form pretreated animals.[19] suggested that water pumping plant from concentrated animal food facilities were the main cause of groundwater contamination with erthyromycin and monensin in USA, Nebraska and concetration reached to 2380 ng/L and 2350 ng/L respectively ,[20] found that sulfadimethoxine and famethazine present in high concertation in the examined groundwater samples with concentrations reached to 0.22 ng/L and 0.068 ng/L respectively.[13] also reported that sufamethazole and sulfathiazole were high in groundwater samples and attribute that to the anerobic condition of water storage which in turn increases ammonia concentration, facilities soil infiltration of these contaminants to the groundwater reservoirs (table1,table 3).

- **Agricultural Soils Contamination**

Contamination of soil with veterinary pharmaceutical commonly occur as result of fertilizing with organic animal manure or through watering with contaminated irrigation water source ,[6] explained the recorded cases of soil contamination in China ,where higher concentration of oxytetracycline, chlortetracycline , sulfonamides and sulfamethazine detected in the soil fertilized with cattle manure, similar results reported by [21], when they detect hazardous quantities of antimicrobial drugs in agricultural farms fertilized with poultry manure and tetracyclines were the most frequent type reached to 0.40 mg/kg ,

Testing of some soil samples found traces of the antibiotic drug enrofloxacin present in quite low amounts. at levels of 0.02 and 0.05 mg per kg of soil were detected. This shows how persistently stable such compounds can be, since the soils were fertilized with manure seven months prior and still contained residuals of the fluoroquinolone medication. [21]

A study of [22] looked at the presence of various antibiotic drug classes - tetracyclines, sulfonamides, trimethoprim and fluoroquinolones - in manure samples from pigs, chickens and turkeys. The tetracycline antibiotic specifically detected in 22 out of 30 pig manure samples, with levels ranging from 0.36 to 23 mg/kg. The researchers propose this finding likely the main cause of soil contamination, since these animals provided with tetracyclines as food additives (table 1,table 4).

## Human health concerns

Veterinary pharmaceutical pass from the environment to the plant and water, lead to contamination of human food source. The overuse of antibiotics in various sectors has led to their widespread presence in the environment. from livestock, aquaculture and agriculture end up in wastewater and soils. Pharmaceutical factories and water treatment plants also contribute to environmental contamination [24].

This exposure plays a role in increasing antibiotic resistance. Bacteria are often subjected to very low antibiotic concentrations in the environment, allowing them to adapt and evolve over time. Mutations from sub-lethal drug amounts seem particularly important for resistance emergence.

Even exposure to non-killing antibiotic levels can cause mutations in bacteria. These changes can accumulate, resulting in strains that are hard to treat [25][26].

Studies found that sub-minimum inhibitory concentrations of certain drugs in E. coli induced mutagenesis. This was linked to increased reactive oxygen species, leading to acquired resistance. Mutations were observed in specific genes associated with antibiotic targets. Resistance also emerged faster following exposure to quinolone levels below standard measurements. Likewise, single mutations gave pathogens 100-times greater tolerance to that drug [27][28].

Veterinary medication residues in foods sources have been shown to cause allergic reactions in humans through consumption. Drugs like penicillin, cephalosporins, and tetracyclines are common culprits, inducing effects ranging from mild rashes to life-threatening anaphylaxis. β-lactams specifically provoke allergic responses. Beyond this, sulfamethazine, oxytetracycline and furazolidone residues carry immunopathological implications as well [29][30].

Teratogenic and carcinogenic impacts are also a concern. Any chemical disrupting fetal development can lead to structural or functional birth defects, as demonstrated for certain anthelminthics, benzimidazoles, and enrofloxacin in animal studies. Meanwhile, antibiotic remnants that bind to or alter intracellular components like DNA may induce cancer over the long run, exemplified by reported chloramphenicol tumors. Nitrofuran, nitroimidazole and quinoxaline residues also interact with cellular molecules in ways that could change DNA and promote oncogenesis [31][32][ 33].

Unintended dietary exposures to veterinary drug residues via foods present immunological, teratogenic and carcinogenic risks to humans through various reaction and toxicity mechanisms within the body. Careful management is important to safeguard public health from public health consequences (table 5).

## Management and environmental control

Limited public understanding about prudent veterinary pharmaceutical use has exacerbated the issue of antibiotic residues polluting the environment. Effective communication is vital to inform people about insignificant usages that negatively impact health [34].

Targeting multiple groups can enhance outreach efforts. Pharmaceutical industries and professional organizations upholding standards can lend great influence. Social influencers also play a pivotal role by legitimizing issues [33][34].

Designing of educational incentives assessed over time may prove impactful, especially training women, economically disadvantaged communities, and those employed in agriculture and fishing. Standard-setting agencies like the WHO and national health bodies initiate important global and local initiatives annually to spread best practices [35].

Events promoting understanding among multifaceted stakeholders concerning antibiotic selection pressures are advantageous. Promoting infection control and ongoing surveillance allows continuously addressing the threat of antimicrobial resistance. A holistic approach engaging an array of relevant players through different mediums remains most promising for building antibiotic stewardship [36][37].

## Conclusion

It is recognized by environmental experts that active drugs and their metabolites have contributed globally to aquatics and land contamination. While the knowledge is growing, large information gaps remain on their effects. The impacts of these chemicals in the environment are still largely unknown. This review shows a clear need to track not just presence of veterinary compounds in different areas worldwide, but primary sources as well. Identifying sources is key to shaping regulatory monitoring, as it addressing current problems and preventing future issues.

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**Table 1:** the common types of pharmaceuticals used in veterinary fields

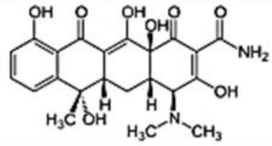
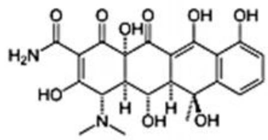
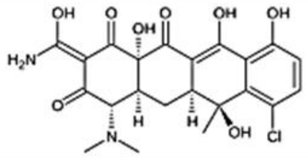
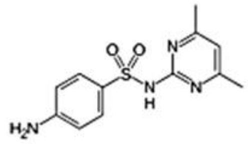
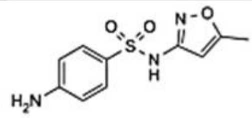
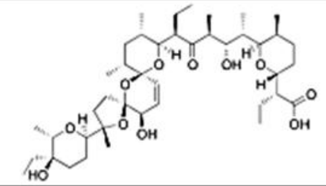
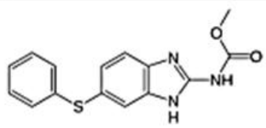
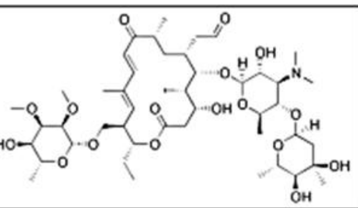
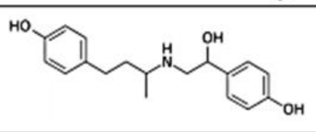
| Class | Compound | CAS-Nr | Structure | Formula |
|---|---|---|---|---|
| Antibiotics | Tetracycline | 60-54-8 |  | $C_{22}H_{24}N_2O_8$ |
| | Oxytetracycline | 79-57-2 |  | $C_{22}H_{24}N_2O_9$ |
| | Chlortetracycline | 57-62-5 |  | $C_{22}H_{23}ClN_2O_8$ |
| | Sulfamethazine | 57-68-1 |  | $C_{12}H_{14}N_4O_2S$ |
| | Sulfamethoxazole | 723-46-6 |  | $C_{10}H_{11}N_3O_3S$ |
| | Salinomycin | 53003-10-4 |  | $C_{42}H_{70}O_{11}$ |
| Anthelmintic | Fenbendazole | 43210-67-9 |  | $C_{15}H_{13}N_3O_2S$ |
| Feed additives | Tylosin | 1401-69-0 |  | $C_{46}H_{77}NO_{17}$ |
| | Ractopamine | 97825-25-7 |  | $C_{18}H_{23}NO_3$ |

**Table 2:** the global reported veterinary pharmaceuticals in surface water sources and their concentrations

| References | Location | Type of pharmaceutical | Concentration | Contamination source |
|---|---|---|---|---|
| Koné *et al* [12]. | Canada | 1- Trimethoprim<br>2- Sulphamethoxazole<br>3- Venlafaxine<br>4- Fluoxetine | 1-3.528 µg/L<br>2- 278 µg/L<br>3- 0.808 µg/L<br>4- 0.799 µg/L | Surface water, sewage treatment plant |
| Bartelt-Hunt *et al* [13]. | USA | sulfamerazine; sulfamethazine; erythromycin; monensin; tiamulin; and sulfathiazole. Lincomycin; ractopamine; sulfamethazine; sulfathiazole; erythromycin; tiamulin and sulfadimethoxine | 30 to 3600ng/L | lagoons and adjacent groundwater |
| Kulik *et al* [14]. | Poland | 1- erythromycin<br>2- vancomycin<br>3- oxytetracycline<br>4- sulfamethoxazole<br>5- clindamycin<br>6- trimethoprim | 1-0.89 ng/L<br>2-2.99 ng/L<br>3-0.27 ng/L<br>4-0.20 ng/L<br>5-0.36 ng/L<br>6-(0.29 ng/L] | surface water |
| Lim *et al* [8] | Korea | chlortetracycline, oxytetracycline, acetylsalicylic acid | 1.85-143.83 µg/L | Sewage water, wastewater plants |
| Matsuin *et al* [16] | Japan | oxytetracycline | 2 ng/L to 68 µg/L | stream waters, catchment water |

**Table 3:** the global reported veterinary pharmaceuticals in ground water sources and their concentrations

| References | Location | Type of pharmaceutical | Concentration | Contamination source |
|---|---|---|---|---|
| García-galán *et al* [17]. | Spain | 19 types of sulfonamides | 0.01 ng/L to 3460.57 ng/L | ground water, wells |
| Bartelt-Hunt *et al* [13]. | USA | Steroid hormones | up to 390ng/L. | groundwater |
| Batt *et al* [18] | USA | Sulfamethazine<br>Sulfadimethoxine | 1- 0.076- 0.215 µg/L<br>2- 0.046 - 0.068 µg/L | ground water wells |
| Fisher *et al* [20] | Australia | sulfadimethoxine and famethazine | 0.22 ng/L and 0.068 ng/L | groundwater |

**Table 4:** the global reported veterinary pharmaceuticals in soil and their concentrations

| References | Location | Type of pharmaceutical | Concentration | Contamination source |
|---|---|---|---|---|
| Wang *et al* [6] | China | Amoxicillin, Albendazole, Ciprofloxacin, Ivermectin, Sulfadimidine, Sulfamethoxazole, Tylosin, Trichlorfon | 49mg/kg | Soil, aquaculture |
| Karcı and Balcıoğlu [21] | Turkey | Tetracyclines, sulfonamides, and fluoroquinolones | 0.05-0.5 mg/kg | spiked soil and manure samples |
| Martínez-Carballo *et al* [22] | Austria | 1- Chlortetracycline,<br>2- oxytetracycline<br>3- Enrofloxacin | 46 mg/kg<br>29 mg/kg<br>90 mg/kg | soils fertilized with manure |
| Slana *et al* [23] | Slovenia | Tiamulin<br>Enrofloxacin<br>Tylosin<br>Sulfadiazine<br>Oxytetracycline<br>Gentamicin | 0.096g/g -0.647g/g | Manure and agricultural soil |

**Table 5**: common antibiotic adverse effect in the contaminant environment [32]

| Class | Type | adverse effect |
|---|---|---|
| Tetracycline | Oxytetracycline | Blood changes, Damage calcium reach teeth &bone, wheezing and asthmatic attack |
| Macrolides | Erythromycin | Pyloric stenosis in infant, sever vomiting, teratogen, hart deformity in infant |
| Amphenicol | Chloramphenicol | Human carcinogenic, genotoxic, toxic to kidney, heart, liver, damage of bone marrow causes plastic anemia |
| B – lactamase | Ampicillin | Hepatitis, allergic action, dermatitis, anemia, thrombocytopenia, leukopenia, asthmatic attack |

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