Antibiotics Pollution in Soil and Water: Potential Ecological and Human Health Issues

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Abbreviations

ARG	antibiotic resistance genes
AHI	Animal Health Institute
CTC	chlortetracycline
DC	doxycycline
DOM	dissolved organic matter
EC50	effective concentration that inhibits growth of 50% of a population
ECTC	epichlortetracycline
ELISA	enzyme linked immunosorbent assay
FDA	Food and Drug Administration
ICTC	isochlortetracycline
Kd	distribution coefficient
LC/MS	liquid chromatography/mass spectrometry
MIC	minimum inhibitory concentration
OTC	oxytetracycline
SCP	sulfachloropyridazine
TC	tetracycline
TCs	tetracyclines
SAs	sulfonamides
US	United Sates
VRE	vancomycin-resistant *Enterococci*
WWTPs	wastewater treatment plants

Introduction

The presence of antibiotic residues in terrestrial and aquatic systems, resulting largely from discharges from municipal wastewater treatment plants (WWTPs) and land application of animal wastes, is now well documented in the literature. Many animal confinement operations generate manure that contains antibiotics because animals receive these drugs in feed rations, either as growth promoters or as therapeutic agents. Treated animals excrete antibiotic metabolites and some nonmetabolized antibiotics, which are then introduced to agricultural lands through repeated fertilization with animal manure. As depicted in Figure 1, veterinary antibiotics are introduced into the soil from manure application. Through surface runoff and leaching, antibiotics and their metabolites can be transported to surface water and groundwater. Similarly, human antibiotics from the effluents of WWTPs are introduced directly into surface water.

In the United States (US) and other developed countries, antibiotics are regularly used not only in human treatment of diseases but also in modern animal agriculture, both as therapeutic drugs to treat and control diseases, and as growth promoters and to improve feed

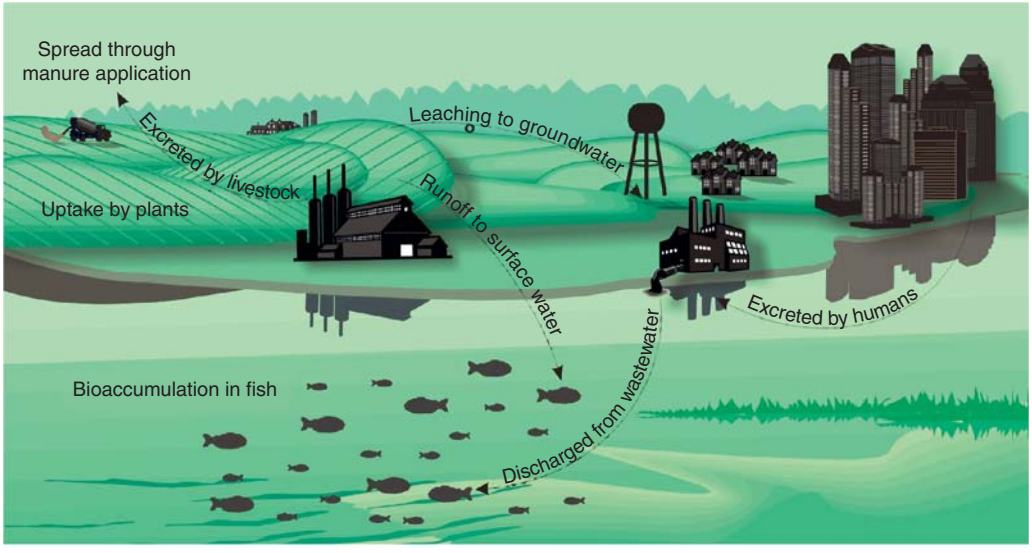


Figure 1 Sources and transport of human and veterinary antibiotics in the environment artwork by Christine Klein.

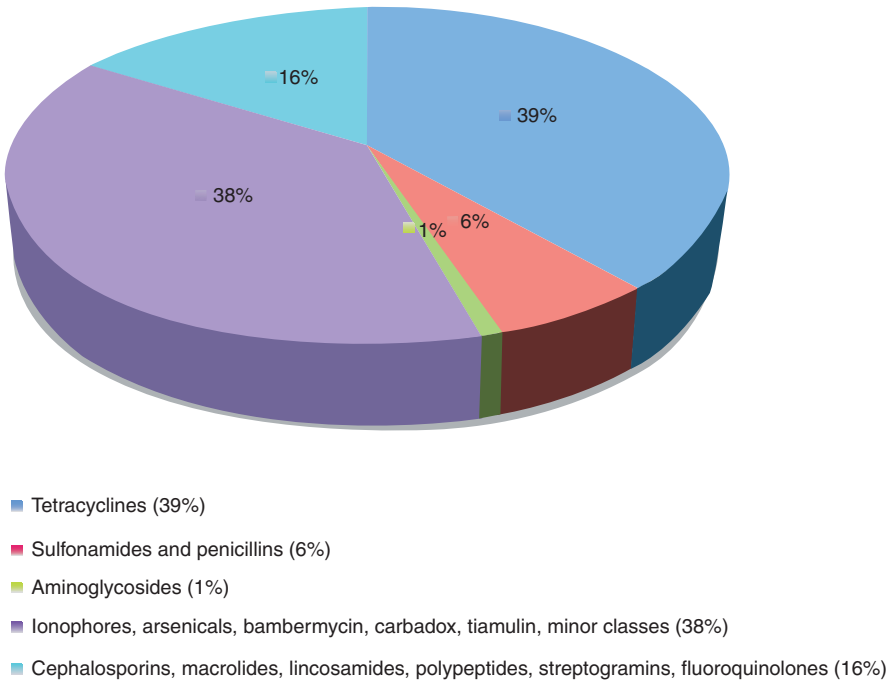


Figure 2 General distribution of antibacterial ingredients sold in 2007 by Animal Health Institute Members in the United States for veterinary use (Source: Animal Health Institute 2008).

efficiency at subtherapeutic levels. A recent survey from the Animal Health Institute (AHI) reported approximately 27.8 million pounds (12.6 million kg) of active antibiotic ingredients sold in the US in 2007, with approximately 13% of these used for growth promotion and increase feed efficiency. The general distribution of major veterinary antibiotics used in the US is shown in Figure 2.

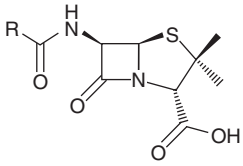
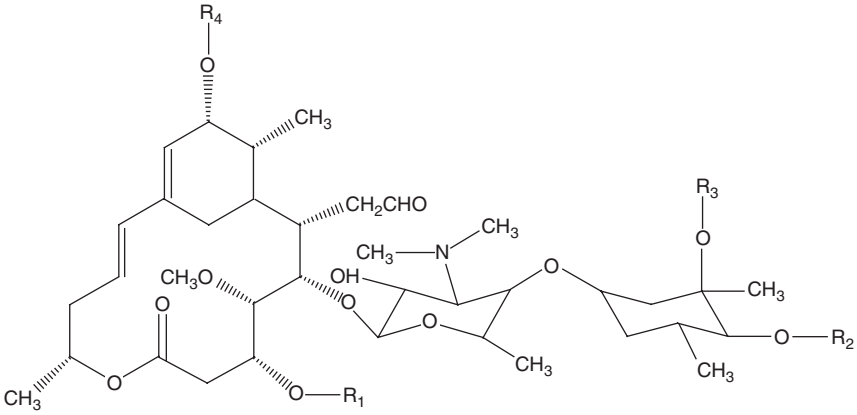
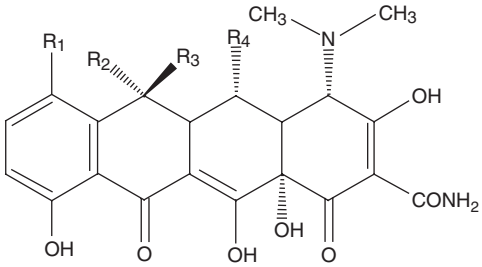
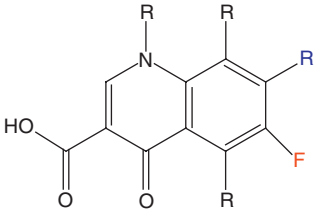
Antibiotics may be classified based on bacterial spectrum (broad versus narrow), route of administration (injectable versus oral versus topical), type of activity (bactericidal versus bacteriostatic), and origin (natural versus synthesized). However, the most useful way of classification is based on chemical structure. Antibiotics within a structural class generally have similar patterns of effectiveness, toxicity, and allergic potential. Table 1 lists different antibiotics that are commonly used in human and animal therapy.

Antibiotics are defined as naturally, semisynthetic, and synthetic compounds with antimicrobial activity that can be applied parenterally, orally, or topically. Many have considered that the discovery of antibiotics is the greatest advancement in the history of medicine. Since discovery in the early 1900s, hundreds of antibiotics have been commercialized and used extensively in human and animal medicine, which account for 40–80% of the total annual usage. At present, antibiotics play a major role in modern agriculture and in livestock industries, and antibiotic use has been on the rise in many developed nations.

Accurate information on the total production and use of antibiotics in the US is limited due to poor documentation by the producers and the lack of public access to records. Hence, there is controversy with regard to the relative amounts of antibiotics that are used for growth promotion versus those that are used for disease treatment and prevention. For instance, the Union of Concerned Scientists issued a report stating that approximately 70% of the estimated 12 million kilograms of antimicrobial compounds used annually in the US are used for nontherapeutic purposes (growth promotion). The AHI, however, reported that only approximately 14% of the 9.6 million kilograms of antibiotics consumed in 1999 were used to improve growth and feed efficiency. In the most recent AHI survey (2008), it was reported that only 13% of the overall antimicrobial sales were used in animal growth promotion. This low percentage recently reported by AHI is contradictory with the high numbers previously reported by the Environmental Media Services and the Institute of Medicine and National Research Council in 1980, which estimated that approximately 40% of antibiotics produced in the US are used as growth promoters or feed supplement.

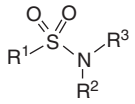
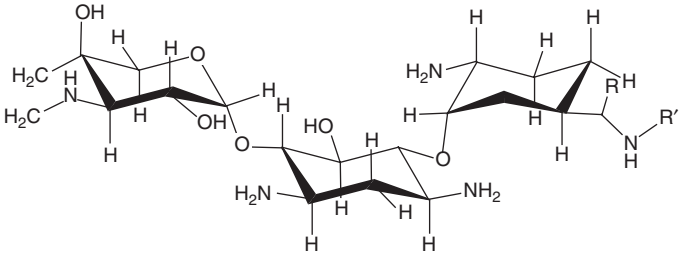
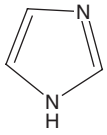
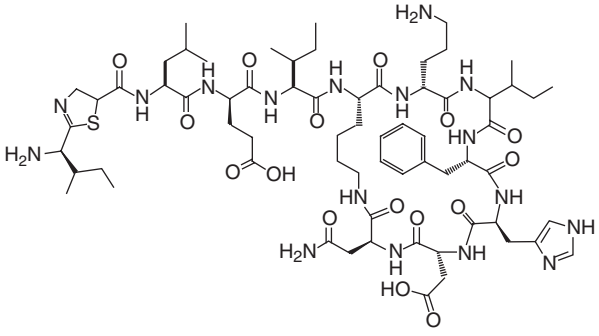
The use of antibiotics as growth promoters in animal production has been a common practice for nearly 60 years now, as a result of their well-recognized beneficial effects on production efficiency in poultry and swine. The use of antibiotics as animal additives or food supplements without veterinary prescription was approved

Table 1 Major classes of antibiotics and their representative structures

Class (chemical structure)	*Mechanism of action*	*Uses*
B-lactam antibiotics 	Inhibition of bacterial cell wall synthesis	Human Animals
Penicillins: penicillin G, amoxicillin *Cephalosporins*: cefoxitin, cefotaxime, *Carbapenem*: imipenem		
Macrolides 	Inhibition of bacterial protein synthesis	Human Animals
Erythromycin, azithromycin, tylosin		Growth promoter
Tetracyclines 	Inhibition of bacterial protein synthesis	Human Animals
Tetracycline, chlortetracycline, oxytetracycline, doxycycline		Growth promoter
Fluoroquinolones 	Inhibition of bacterial DNA synthesis	Human Animals

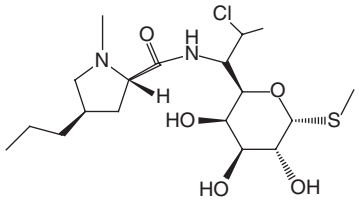
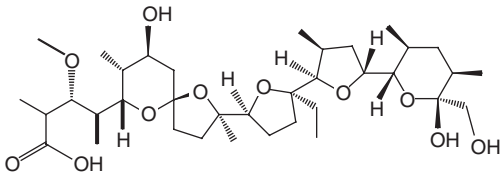
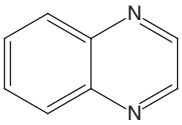
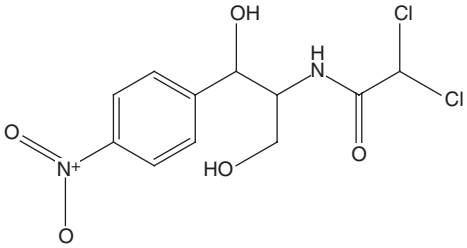
(*Continued*)

Table 1 Continued

Class (chemical structure)	*Mechanism of action*	*Uses*
Norfloxacin, ciprofloxacin, enoxacin, ofloxacin		
Sulfonamides	Blocks bacterial cell metabolism by inhibiting enzymes	Human Animals
		
Sulfadiazine, sulfamethoxasole, sulfapyridine		Growth promoter
Aminoglycosides	Inhibition of bacterial protein synthesis	Human Animals
		
Gentamicin, amikacin		
Imidazoles	Inhibition of bacterial DNA synthesis	Human Animals
		
Metronidazole		Growth promoter
Peptides	Inhibition of bacterial cell wall synthesis	Human Animals
		

(*Continued*)

Table 1 Continued

Class (chemical structure)	*Mechanism of action*	*Uses*
Bacitracin		Growth promoter
Lincosamides	Inhibition of bacterial protein synthesis	Human Animals
		
Clindamycin, lincomycin		
Ionophores	Blocks intracellular protein transport	Animals Growth promoter
		
Monensin, lasalocid		
Quinoxalines	Inhibition of bacterial DNA synthesis	Human Animals
		
Carbadox, olaquidox		Growth promoter
Other	Inhibition of bacterial protein synthesis	Human Animals
		
Chloramphenicol		

by the US Food and Drug Administration (FDA) in 1951. The mechanism of the antibiotic growth promoting action has been suggested to be due to the reduction in microbial metabolites that depress growth in the gut of the animal. Another mechanism could be due to the reduction in gut size from the loss of mucosa cell proliferation in the absence of luminal short chain fatty acids derived from microbial fermentation that enhance

nutrient digestibility. The prevalence of antibiotic use, especially at subtherapeutic levels, has raised concerns with regard to their long-term detrimental effects on the ecological balance in the environment.

Environmental Fate of Antibiotics: Focus on Tetracyclines and Sulfonamides

Studies on the environmental fate of antibiotics have emerged as an important research topic in the past decade. Human antibiotics are released into the environment mainly by excretion, flushing of old and out-of-date prescriptions, and medical wastes from hospitals, which may all go to WWTPs. The animal antibiotics, however, enter the environment in several ways, with the runoff from manure-treated farmland as the primary pathway. Other pathways include direct application in aquaculture, wash-off from topical treatments, and livestock waste treatment plants. The fate of these antibiotics once in the environment depends on their physicochemical properties, prevailing climatic conditions, soil types, and a variety of environmental factors.

Owing to the vast literature on antibiotics pollution to date, the discussion in this article will focus only on the two most widely used antibiotics in the world, especially in animal production, namely, tetracyclines (TCs) and sulfonamides (SAs). TCs, before the advent of arsenicals and ionophores antimicrobial agents, were the most used antibiotics in animal therapy. Chlortetracyline (CTC), oxytetracycline (OTC), tetracycline (TC), and doxycycline (DC) are the commercially available TCs on the market. SAs, however, are one of the oldest groups of antibiotics with use dating back to the 1930s. Representative SAs include sulfanilamide, sulfamethazine, sulfadiazine, sulfadimethoxine, sulfapyridine, sulfachloropyridazine, and sulfamethoxazole. Sulfamethoxazole in combination with trimethoprim is one of the most commonly used antibiotic prescriptions for human therapy.

Tetracyclines in Soil

The use of animal manure as fertilizer is a significant point source of antibiotic pollution to the environment. It has been reported that TC-treated animals excrete between 70% and 90% of the antibiotics administered via urine and feces. In cows, 75% of ingested chlortetracycline and 23% of ingested OTC are recovered in manure. Although in pigs, up to 72% of TCs were recovered in the feces and urine. TCs in manure can undergo transformations depending on the pH of the surroundings. The degradation products that are formed may have either lower or higher biological activities than the parent compound.

The amounts of antibiotic residues in manure can vary widely, depending on the animal species and their age. In liquid manure from livestock farms, concentrations of approximately 4.0 mg kg^{-1} TC and 0.1 mg kg^{-1} CTC have been reported. Another study of the same group showed concentrations of 0.011 and 1.435 mg kg^{-1} CTC in cattle manure slurry and pig manure slurry, respectively. Higher concentrations of TCs were observed in dung from beef cattle. Others have reported CTC, ECTC (epichlortetracycline), and ICTC (isochlortetracycline) concentrations of 281, 157, and 67 mg kg^{-1} in pigs, respectively, after 10 days of CTC medication.

TCs in general are persistent in soil. For instance, an average concentration of 9.5 μg kg^{-1} CTC was detected in the upper 10 cm of the soil from fields that had been manured with animal slurry 2 days before sampling. In the same study using soils with conventional land farming, average concentrations of up to 199 μg kg^{-1} TC and 7 μg kg^{-1} CTC were detected during the 2 years of monitoring. Results from an antibiotic leaching field study showed no OTC in the 20–30 cm depth soil sample or the leachate, which suggests that OTC remains fixed in the upper soil.

In another field study, OTC was detected only in the top 0–5 cm of the soil cores at concentrations of 27 and 94 μg kg^{-1} in the two lysimeters where slurry was incorporated, and at concentrations of 19 and 41 μg kg^{-1} in the two lysimeters where slurry was applied to the surface. In a separate study, similar results were observed in manure-amended soils, where 270 μg kg^{-1} OTC were detected 3 weeks after application, and 3.6 μg kg^{-1} OTC detected after 4 months, in the surface soil (0–5 cm). These results are consistent with the reported high soil/water distribution (Kd) coefficients of TCs in soils. Reported Kd values of TCs vary from 290 to 1620 in comparison to the SAs whose values range from 0.6 to 4.9. The Kd values are critical parameters in risk assessment of antibiotics because Kd values are related to the leaching potential of chemicals to groundwater.

However, other factors also influence the sorption of antibiotics in soil. The humic complexes either mask sorption sites in clay surfaces or inhibit interlayer diffusion of TCs. It was also observed that in seawater, OTC could bind with calcium and magnesium, reducing the antibacterial activity of OTC.

Studies have shown that TCs are tightly bound to clay minerals and form strong complexes with the cations in clay. The mechanisms of adsorption/desorption of TCs in soils and clays have been investigated extensively. For instance, it has been shown that the adsorption of OTC in montmorillonite clay is governed by cationic exchange interactions at lower pH and that hydrophobic interactions are less important. However, large concentrations of dissolved organic matter (DOM) decrease OTC sorption, suggesting that TCs could be mobilized in soil environments that are rich in DOM, such as in manure-amended

soils. Adsorption of TCs on clay can be reversible; they can be released under appropriate pH and ionic strength conditions making them available to interact with soil bacteria for long period of time. Therefore, it is not surprising that TCs have been detected in the aquatic environments. OTC concentrations ranging from 0.1 to 11 $\mu g\,g^{-1}$ have been reported in sediments under a marine salmon farm, whereas TCs have been detected in groundwater samples collected near waste and wastewater lagoons ($>1\,\mu g\,L^{-1}$), and liquid hog lagoon samples (5–700 $\mu g\,L^{-1}$).

In the environment, manure-borne OTCs can be transformed into derivatives that persist in soil. In a field study using an enzyme-linked immunosorbent assay (ELISA) to determine the antibiotic residues in soil, the amounts of TC-like compounds detected by ELISA showed high concentrations persisting in soil even after 16 months of manure application. In contrast, when the results were verified by a more specific method, using liquid chromatography/mass spectrometry (LC/MS), the OTC concentrations disappeared in surface soil over a short period of time. The large differences between ELISA and LC/MS results suggest that unidentified degradates formed in soil are binding to the ELISA antibodies that have broad specificity. The antibody cross-reactivity profile showed that many TC derivatives containing the basic conjugated ring structure produce a positive assay response. Hence, it is conceivable that there are numerous unknown OTC transformation products in soil extracts that caused the ELISA response to be higher in comparison to the target-specific LC/MS method. In this context, the information gained from ELISA is very important because it indicates the presence of TC-related residues in soil that remain undetected using LC/MS.

Sulfonamides in Soil

Animals excrete between 50% and 100% of the administered dose of SAs within several days of treatment. A total concentration of 20 $mg\,kg^{-1}$ SAs has been found in pig manure, and as high as 300–900 $mg\,kg^{-1}$ of sulfadimethoxine in fresh feces from treated calves has been detected. Another study reported 11–80 $\mu g\,kg^{-1}$ sulfadiazine, 10–270 $\mu g\,kg^{-1}$ N4-acetylsulfadiazine, and 11–62 $\mu g\,kg^{-1}$ sulfadimidine in pig manure. The composition of excreted SAs may contain approximately 30–95% parent compounds, and between 5% and 60% acetylated conjugates. Another metabolite excreted by sulfadiazine-treated animals is 4-hydroxysulfadiazine, which has been shown earlier to exhibit antimicrobial activity. Conjugated metabolites can be reverted back to their parent compounds during manure storage and on application of manure to soil. Therefore, it is critical that metabolites and degradation products are included in fate and transport studies, and in risk assessment of antibiotics in the environment.

In general, SAs have high water solubilities and low Kd values, indicating high mobility in soil. Therefore, it is not surprising that SAs are more likely to be present in the aquatic systems relative to TCs. SAs have been found in river water, groundwater, wastewater, water wells, and even in drinking water. Laboratory and field studies on the sorption behavior of sulfachloropyridazine (SCP) and sulfamethazine demonstrated the high leaching potential of these antibiotics in soil. A field study using animal manure slurry showed the presence of SCP in the leachate (0.51 $\mu g\,L^{-1}$) 35 days after application. In another study involving the transport and dissipation of SCP in sandy loam soil, it was found that SCP dissipated more rapidly than OTC, which is consistent with their relative Kd values. The SCP concentrations in surface runoff samples were found to be 325.9 $\mu g\,L^{-1}$, and in soil water samples at 40 cm depth the concentration was 0.78 $\mu g\,L^{-1}$ after 20 days of application. In a recent study using typical agricultural conditions, SCP was also detected in the leachate. However, some studies reported manure-amended soil containing SA concentrations ranging from 0.015 to 0.40 $mg\,kg^{-1}$.

The presence of manure matrix influences the fate and transport of SAs in the environment significantly by increasing runoff volume and enhancing chemical mobilization potential. Manure increases the runoff volume up to six times compared with the controls due to the physical sealing of the soil surface. The DOM in manure is also an important factor because it reduces the affinity of SAs to soil and induces colloid-facilitated transport. In addition, the SAs can be immobilized because of binding with organic materials such as compost, humic acids, inorganic sorbents such as iron hydroxide, or clay minerals. The sorption of SAs becomes more pronounced as the contact time with the sorbents is prolonged.

Sorption of SAs in soil is complex and may involve cross-coupling with organic matter constituents of soil. Sorption is also influenced by various factors such as pH, ionic strength, exchangeable cations, and the content and composition of soil organic matter. Research showed the presence of SAs in groundwater down-gradient from an animal feeding operation at concentrations ranging from 0.046 to 0.22 $\mu g\,L^{-1}$. SAs were detected in wells as deep as 16 m, suggesting that unlike TCs, sorption of SAs in soil is low. However, a soil leaching study did not show detectable amounts of SAs in lysimeters and attributed these findings to degradation. But, research showed that the biodegradability of SAs is slow even in media with a high microbial population, such as activated sludge. Therefore, it can be inferred from these studies that abiotic processes are significant for the elimination of SAs in soil. These gaps in knowledge need to be addressed because SAs are highly mobile, and their persistence in

the environment could pose potential long-term ecological risks.

Ecological Impacts of Antibiotics and Resistant Bacteria

The environmental contamination by antibiotics may have profound ecological effects at several levels, but the increased emergence and distribution of antibiotic resistance in pathogenic bacteria is by far the most important issue. This is because constant exposure to antibiotics provides an environment that is conducive for selective pressure toward antibiotic-resistant microorganisms and the antibiotic-resistance genes (ARG) that they carry. Even very low concentrations of antibiotics and their metabolites may potentially stimulate ARG. Thus, the concentrations of antibiotics in surface water and other environmental compartments, which are generally below known toxicity and minimum inhibitory concentration (MIC) thresholds, may still induce ARG and contribute to resistance. In fact, numerous studies have documented elevated levels of resistance and ARG in environments adjacent to livestock operations, including runoff, surface water, irrigation ditches, and groundwater.

The effectiveness of antibiotics has diminished over the years. The World Health Organization, the US Center for Disease Control, and numerous other global and national agencies recognize that the rate of antibiotic resistance among many disease-causing bacteria has been increasing every year. For example, killer pathogens such as multidrug-resistant tuberculosis, methicillin-resistant *Staphylococcus aureus*, and vancomycin-resistant *Enterococci* (VRE) have caused approximately 98 000 deaths per year from hospital-acquired infections in the US, which is a notable increase from 13 300 deaths in 1992. According to most recent estimates, 70% of all hospital-acquired infections are resistant to at least one class of antibiotics.

Antibiotics in the environment also affect the microbial community structure and activity, functional microbial community, and other organisms in soil and water. Initial reports show inconsistency with regard to the ecological effects of antibiotics. For example, in an earlier study it has been shown that microbial growth and activity promotion resulted from exposure to OTC- and CTC-containing beef feces because of the higher carbon source in the soil when these antibiotics are present. However, in another study where a combination of OTC and penicillin antibiotics were applied to forest soils, a significant reduction in the populations of both target and nontarget organisms such as bacteria, fungi, protozoa, and nematodes was observed.

A study on the effects of sulfapyridine and OTC on soil microbial activity and microbial mass made use of different parameters such as basal respiration, dehydrogenase activity, substrate respiration, and Fe (III) reduction to determine the effect of antibiotics on microbial activity. Although antibiotics showed no effect on the basal respiration and dehydrogenase activity of soil microorganisms, the substrate respiration showed time-dependent effects of the antibiotics and clear dose–response relations when the incubation time was extended.

Even small concentrations of antibiotics can cause significant effects on the population of soil microorganisms (i.e., reduction in the number of soil bacteria). In addition, the diversity of soil bacterial population can be reduced, whereas the soil fungi could increase and dominate the microbial biomass. Another study, using an OTC–penicillin combination, led to the reduction in the soil bacterial biomass and, at the same time, a reduction in active fungal hyphae. Another study showed that a single addition of sulfadiazine in combination with manure had long-term effects on the microbial community structure and function in soils. In terms of microbial community structure, sulfadiazine has no effect on the Gram-negative to Gram-positive ratio, but addition of manure causes shifts toward the fungi. Tylosin was also found to affect soil bacterial community structure by shifting from a Gram-positive to Gram-negative-dominated community.

The impact of antibiotics on soil microbial and enzymatic activity has been assessed using soil respiration and phosphatase activity tests. Although TCs and tylosin did not significantly affect soil microbial respiration, SAs (sulfamethoxazole and sulfamethazine) and trimethoprim were found to cause a significant decrease in respiration within the first 4 days. However, the rate of respiration increased after 4 days, probably due to the loss of antibiotics from degradation. Similar observations were also reported in separate studies, where soil microbial respiration recovered and increased over time due to the decrease in bioavailable antibiotics and the subsequent adaptation of microorganisms in the antibiotic-containing environments.

Antibiotic contamination could affect the functional microbial community in terrestrial and aquatic systems. The microbial toxicity of two broad-spectrum antibiotics (chloramphenicol and OTC) was monitored on cultures of nitrifying activated sludge. Although no significant change on the biofilm structure or nitrification rates were observed at 10–250 $mg\,L^{-1}$ chloramphenicol levels applied to the culture, OTC biofilm sloughing occurred at 10 $mg\,L^{-1}$, and nitrification was inhibited at 100 $mg\,L^{-1}$ OTC. In another study, erythromycin, clarithromycin, and amoxicillin were found to significantly reduce the rate of denitrification at 1000 $\mu g\,L^{-1}$, whereas amoxicillin/clavulanic acid and ciprofloxacin have no effect on the denitrification rate. Antibiotics such as ampicillin, benzylpenicillin, novobiocine, OTC, and chloramphenicol were evaluated on a

stabilized nitrifying activated sludge systems under aerated and lithoautotrophic conditions and results showed no effect from the presence of antibiotics on the biomass and nitrate production. Among the pharmaceuticals used in another study, ofloxacin and sulfamethoxazole showed significant inhibition on nitrification.

Studies involving the impact of antibiotics on methanogenesis have also been reported. The effects of six pharmaceuticals (carbamazepine, sulfamethoxazole, propranolol hydrochloride, diclofenac sodium, ofloxacin, and clofibric acid) on the anaerobic digestion process showed that pharmaceuticals caused a mild inhibition to methanogenesis, and the inhibition was directly related to the extent of sorption of the pharmaceuticals to the biomass. In a related study, selected antibiotics significantly inhibited methane production relative to non-amended controls, indicating that antibiotics at concentrations commonly found in swine lagoons can negatively impact anaerobic metabolism.

Other microbial processes may be impacted by antibiotics as well. For example, the effects of antibiotics on carbon source utilization have been reported in some studies. Ciprofloxacin was found to significantly inhibit pyrene mineralization in marine sediments. Ciprofloxacin together with two other pharmaceutical products, triclosan (antiseptic) and tergito NP10 (surfactant), affected individually the rate of algal biomass production and algal community structure. Two samples, one collected upstream and the other downstream of a WWTP, were used and inoculated with natural stream algae. Ciprofloxacin at an initial concentration of $0.15\,\mu g\,L^{-1}$ was employed. There was no significant difference between upstream and downstream samples in terms of algal biomass growth rate as determined by chlorophyll content. However, bioassay tests showed that *Synedra* (plankton) and *Chlamydomonas* (green algae) growth were significantly different for upstream and downstream samples. In follow-up experiments, ciprofloxacin caused a significant increase in the *Synerda* growth at the exposure of 0.012 and $0.12\,\mu g\,L^{-1}$, whereas it caused a decrease in the *Navicular* (algae) growth at $0.12\,\mu g\,L^{-1}$. These results demonstrated that continuous ciprofloxacin presence could influence the algal community structure and shift food web structure of streams.

The deleterious effects of antibiotics on nontarget organisms may be synergistic when antibiotics are in mixture with other antibiotics or compounds. The growth-inhibiting and binary joint effects of 12 antibacterial agents on the freshwater green alga *Pseudokirchneriella subcapitata* (Korschikov) Hindak were investigated over 72-h exposures in one study. Potentially synergistic effects were observed in binary mixtures of the same class antibiotics, such as macrolides, TCs, and fluoroquinolones, as well as in some combined drugs, such as trimethoprim and SAs or tylosin and TCs. In another study, synergistic effects were observed when combinations of erythromycin and OTC were tested on activated sludge microorganisms. Results from the same study obtained higher combined effects than the predicted effects based on the assumption of concentration addition.

The toxicity of tylosin and OTC was tested on soil fauna including earthworms, springtails, and enchytraeids. Neither antibiotic had observable effects on any of the test organisms at environmentally relevant concentrations. The EC_{50} (effective concentration that inhibits growth of 50% of a population) was evaluated for several antibiotics using two species of microalgae, *Microcystis aeruginosa* (freshwater cyanobacteria) and *Selenastrum capricornutum* (green algae), employing the pour plate method. The EC_{50} of the same set of antibiotics was also determined for activated sludge bacteria and *Nitrosomonas europaea*. In general, CTC and oxolinic acid were the most toxic antibiotics to activated sludge and nitrifying bacteria. Overall, *Microcystis aeruginosa* is more vulnerable to antibiotics relative to *Selenastrum capricornutum*. The above-mentioned studies demonstrate that antibiotic concentrations in the low $\mu g\,L^{-1}$ range can affect the structure and function of microorganisms in wastewater and surface water.

Occurrence in Drinking Water Sources and Potential Human Health Risks

The introduction of treated domestic wastewater into water resources is common in urban areas. In addition, several water-recycling programs are being operated in the US. Worldwide, the introduction of wastewater effluent into drinking water aquifers is a critical undertaking to meet the potable water need of heavily populated areas. The increased reuse of treated wastewater has been mirrored by increased concern that antibiotics, resistant bacteria, and ARGs are being introduced into the drinking water systems. Antibiotics and ARGs have been found in finished drinking water and drinking water distribution systems. The presence of ARGs in drinking water systems poses human health risks because of the potential for horizontal gene transfer to pathogenic bacteria. For example, ARGs against ampicillin, streptomycin, and TC are known to be transferable to other bacteria.

Studies have shown that some antibiotic-resistant microorganisms can survive chlorination and in turn can be introduced in the drinking water systems. Strains of *Pseudomonas aeruginosa* that survived chlorination for water treated for drinking purposes were found to be resistant to almost all the antibiotics tested. Another study used ampicillin- and trimethoprim-resistant *Escherichia coli* strains isolated from sewage sludge and subjected them to chlorination, which showed resistance

Table 2 List of some reported effects of antibiotics pollution in soil and water

Observed effects	*References*
Promotion of microbial growth and activity	Patten et al. 1980
Population reduction in target and nontarget organisms	Thiele-Bruhn and Beck 2005; Colinas et al. 1994
Negative effect on soil biomass and microbial activity	Thiele-Bruhn and Beck 2005
Altered microbial community structure in soils observed as long-term effects	Hammesfahr et al. 2008
Shifted soil bacterial community structure from a Gram-positive to Gram-negative-dominated community	Westergaard et al. 2001
Negative growth effects on *Synedra* (plankton) and *Chlamydomonas* (green algae)	Wilson et al. 2003
Deleterious effects on soil microbial and enzyme activity	Liu et al. 2009; Demoling et al. 2009; Kotzerke et al. 2008
Biofilm sloughing and inhibition of nitrification	Campos et al. 2001
Reduction in the rate of denitrification	Constanzo et al. 2005; Dokianakis et al. 2004
Inhibition of microbial metabolism in anaerobic lagoons	Loftin et al. 2005
Inhibition of methanogenesis/methane production	Fountoulakis et al. 2004; Loftin et al. 2005
Reduction in carbon source utilization	Schmitt et al. 2005; Maul et al. 2006
Inhibition of pyrene mineralization in marine sediments	Naslund et al. 2008
Promotion of the occurrence and spread of antibiotic-resistant bacteria and antibiotic-resistance genes in water resources	Kummerer 2004
Promotion of heterotrophic antibiotic-resistant bacteria and antibiotic-resistance genes in finished water and tap water	Xi et al. 2009
Contributes to the occurrence of *Escherichia coli* isolates that are resistant to ampicillin, streptomycin, and tetracycline in drinking water	Walia et al. 2004

against chlorine. These findings support an earlier study indicating that chlorination increases the proportion of antibiotic-resistant and potentially pathogenic microorganisms. In addition, it was reported that 55% of *E. coli* isolates recovered from chlorinated drinking water are resistant to several antibiotics. Further investigations on the combined ecological and human health effects of antibiotics and ARG in drinking water are warranted now that the presence of some antibiotics like sulfamethoxazole, macrolides and quinolones have been detected in chlorinated drinking water and drinking water sources. A summary of some of the reported effects of antibiotics residues in the environment on nontarget organisms is presented in Table 2. Although this table is not comprehensive, it gives a good flavor of the wide range of negative effects that have already been observed as a result of antibiotics contamination of the environment.

Although the concentration of antibiotics in surface waters is very low to exhibit any kind of acute toxicity, many people remain concerned about the presence of pharmaceutical compounds in drinking water because drugs are designed to affect specific protein targets at relatively low doses. For example, the analgesic diclofenac has been reported to dramatically decline the populations of vultures in India and Pakistan. Additionally, it is now well known that the synthetic estrogen, 17 α-ethinylestradiol, used in birth control pills strongly contributes to the feminization of fish even at concentrations below 5 ng L^{-1}.

Although the human toxicities associated with pharmaceuticals and metabolites are mostly known because they have been determined during several years of clinical trials of the drug, knowledge on the ecological toxicity of these compounds when present in the environment is scarce. As a result of the increased detection of pharmaceutical compounds in aquatic systems, many pharmaceutical companies and environmental scientists are investigating the potential effects of trace levels of active pharmaceutical ingredients in surface waters on human health and the environment.

Various investigations involving human health and environmental risk assessments have been reported for pharmaceuticals based on their risk quotients, defined as the ratio of predicted environmental concentrations to the predicted-no-effect concentrations. Although some studies concluded that the levels of pharmaceutical compounds present in the environment are very low and present negligible risks to humans, others claim that certain pharmaceuticals, especially antibiotics, are of high concern for the aquatic environment. It is clear that data are lacking on the chronic effects of pharmaceuticals and their metabolites in the environment, making it difficult to conduct accurate risk assessment using existing models and there are disagreements in the conclusions of risk assessments conducted to date.

Summary and Conclusion

Several investigations have documented the widespread occurrence of antibiotics in various environmental compartments that are impacted by both human and animal

wastes. Although it is known that the physicochemical properties of antibiotics play an important role in their fate, transport, and toxicity, the importance of metabolites and degradation products has been somewhat underestimated in many studies. For a more comprehensive risk assessment, pharmaceutical metabolites should be considered as well because of their potential to contribute synergistically on the toxicity of the parent compounds. The detection of pharmaceuticals in drinking water, despite at trace concentrations, had caused increased concern regarding the potential human health effects of the long-term exposure to these bioactive compounds. In contrast to the more publicized issue, linking the contribution of antibiotics pollution to the increased emergence of antibiotic resistance bacteria, many researchers remain skeptical about the potential human health effects caused by low levels of pharmaceuticals in the environment. There is continuous debate whether the low concentrations of pharmaceuticals detected in drinking water are enough to cause potential environmental and human health issues. Nevertheless, there is enough evidence to show that antibiotics do have deleterious impacts on microbial community structure and function when exposed to such low concentrations of pharmaceuticals. Presently, many wastewater and drinking water treatment utilities are reexamining current infrastructures to improve the efficiencies of removal of pharmaceuticals and other organic microcontaminants in the aquatic systems. Many government agencies are also evaluating the use of antibiotics in the animal industry. Several European countries have already banned the use of antibiotics that are important in human treatment in animal feeds. In the US, stakeholders believe that restricting the use of antibiotics in agriculture is not warranted and is not supported by science. Many federal and private agencies believe that more research is needed before decisions can be made regarding further regulation or restriction of antibiotic use in food animals to achieve sustainability of agriculture, the environment, and human health.

See also: Advances in Analytical Methods for the Determination of Pharmaceutical Residues in Waters and Wastewaters, Groundwater and Soil Pollution: Bioremediation, Lebanon: Health Valuation of Water Pollution at the Upper Litani River Basin, Pharmaceuticals: Environmental Effects, Pharmaceuticals in Drinking Water, Soil Quality Criteria for Environmental Pollutants, Sustainable Management of Agricultural Systems: Physical and Biological Aspects of Soil Health.

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