

Chapter 2

Residual Veterinary Pharmaceuticals in Animal Manures and Their Environmental Behaviors in Soils

Weiping Song and Mingxin Guo

Abstract The worldwide heavy use of veterinary pharmaceuticals in confined animal-feeding operations has resulted in annual discharge of 3,000–27,000 tons of drug chemicals via livestock manure into the environment. More than 50 major antibiotics have been detected in poultry, swine, cattle, and horse manures at 0.01–765 mg kg⁻¹ dry manure mass. In animal manures, most veterinary pharmaceuticals degrade rapidly via biochemical reactions, demonstrating a half-life time 2–30 days. In soils, veterinary pharmaceuticals interact with soil minerals, organic matter, and organisms and are subject to sorption, photohydrolysis, oxidation, and biodegradation. The soil distribution coefficient (K_d) values of animal pharmaceuticals range from 0.3 to 6,300 L kg⁻¹, varying with the chemical species and soil properties. The persistence of veterinary pharmaceuticals in soils is influenced by soil type, organic matter content, pH, moisture content, and temperature. Though certain antibiotics such as roxithromycin, sarafloxacin, and virginiamycin are persistent, the vast majority of veterinary pharmaceuticals are degradable (half-life <30 days) in soils. The sorption, rapid degradation, and physical attenuation limit residual pharmaceuticals in the top 30-cm soil of agricultural land at generally less than 1 µg kg⁻¹, posing little impacts on soil microorganisms, fauna, and plants. Nevertheless, veterinary pharmaceuticals could migrate from manured fields to water bodies via surface runoff and leaching. In North American drainage ditches and streams, up to 290 ng L⁻¹ of animal antibiotics had been detected, although the concentrations were far below the no-observed-effect concentration levels of veterinary pharmaceuticals to aquatic organisms. Antibiotic-resistant bacteria have been identified in animal manures and livestock-handling workers, indicating the risk of antibiotic-resistant genes spread in association with

W. Song

Department of Chemistry, Delaware State University, Dover, DE 19901, USA

M. Guo (✉)

Department of Agriculture and Natural Resources, Delaware State University,
Dover, DE 19901, USA

e-mail: mguo@desu.edu

veterinary pharmaceutical overuse and manure disposal. Future research should focus on developing standard composting protocols to eliminate residual veterinary pharmaceuticals and antibiotic-resistant pathogens from animal manures and on cultivating animal-feeding methods alternative to drug administration.

2.1 Introduction

Veterinary pharmaceuticals are chemical drugs administered to domestic animals to treat diseases, prevent infections, increase weight gain, or improve feed efficiency. Common veterinary pharmaceuticals include antibiotics, antiparasitics, anti-inflammatory medicines, anesthetics, pain relievers, and specialized products used to manage animal reproductive or metabolic conditions. These medications are prepared in a variety of forms such as pills, liquids, injections, or powders and can be applied to animals via feed or drinking water, by injection or skin insertion, or simply through drenching (OTA 1979).

The U.S. confined animal feeding operations rely heavily on veterinary pharmaceuticals to maintain healthy, productive livestock. Veterinary antibiotics are regular feed supplements of poultry, swine, cattle, equine, and aquaculture (Henderson and Coats 2010). Considering chemical structures, most veterinary pharmaceuticals are amphiphilic or amphoteric, ionizable organic compounds consisting of a nonpolar core and multiple polar functional groups (Thiele-Bruhn 2003). After imposed to livestock, these pharmaceuticals are typically absorbed through animals' digestive and circulatory systems and discharged in waste from the excretory system. The pharmaceuticals are generally metabolized and deactivated for biological functions after the animal body passage. A significant portion (10–90 %) of the applied quantities, however, may remain intact as parent compounds and deposit in animal tissues and excrement (Kumar et al. 2005a). Certain metabolites are also biologically active (Halling-Sørensen et al. 1998). Residues of veterinary pharmaceuticals and their active metabolites in animal tissues and excreta have been exclusively detected (Kumar et al. 2005a; Furtula et al. 2010). Responding to the residual pharmaceuticals, microorganisms such as *Enterococcus* spp., *Staphylococcus* spp., and *E. coli* in animal manures may develop antibiotic resistance (Hayes et al. 2004; Furtula et al. 2010). Through land application of animal waste as an organic fertilizer, these residual veterinary pharmaceuticals and antibiotic-resistant microorganisms enter into soil and water and may influence aquatic ecosystem and accumulate in food crops (Solomon et al. 2010; Carlsson et al. 2013). To assess the potential risks posed by veterinary pharmaceuticals from land application of animal waste, the occurrence of animal drug compounds in animal manures and their fate and transport in agricultural ecosystems need to be addressed. This chapter is to summarize veterinary pharmaceutical uses in confined animal feeding operations, reports on presence and detection of residual veterinary medicines in manures, and review the environmental behaviors of pharmaceutical residues in agricultural soils.

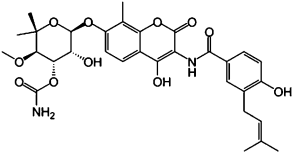
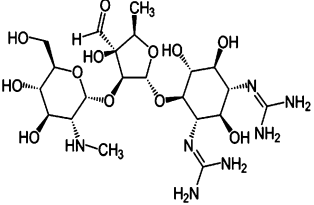
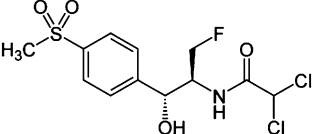
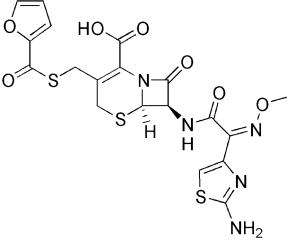
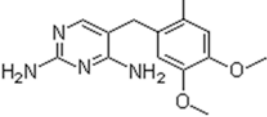
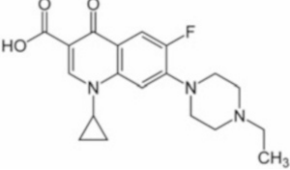
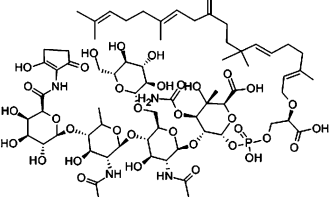
2.2 Uses of Veterinary Pharmaceuticals in Animal Production

More than 400 active chemical ingredients have been manufactured into nearly 2,000 veterinary pharmaceutical products to treat various species of animals including pigs, cattle, horses, sheep, goats, birds, fish, deer, cats, and dogs (FDA 2012). These chemicals are conventionally placed into five groups: anthelmintics (dewormers), tranquilizers, antibiotics, hormones, and agonists. According to their functions, they can be further categorized as therapeutic medicines (to treat animals for preventing diseases, combating infections, or alleviating pain or injury. Examples include coccidiostatics, trimetoprim, and sulfamethizol) and growth promoters (to help with animal feed digestion and growth efficiency. Examples are tylosin, monensin, and virginiamycin) (Garrido Frenich et al. 2010).

More than 70 % of the consumed veterinary pharmaceuticals are antibiotics – chemicals that can inhibit the growth of other microorganisms even at extremely low concentrations (Halling-Sørensen et al. 1998). There are over 150 antibiotics in use today, of which more than 90 % are natural products of bacteria and fungi (molds) and semisynthetic modifications of natural compounds, and a few such as sulfonamides are completely synthetic (von Nussbaum et al. 2006). The first commercially manufactured antibiotic was penicillin, a chemical compound derived from *Penicillium* fungi. Antibiotics were initially and are continuously used for therapeutically treating human and animal diseases and infections. In 1949, the U.S. officially approved the use of antibiotics as a feed additive in the rearing of domestic animals for human consumption, so did the United Kingdom in 1953 (Witte 2000). Today, supplementing animal feed with antibiotics has been practiced in nearly all livestock and aquaculture operations in most countries. Antibiotics added in feed serve predominantly as growth promoters. It is believed that the antibiotics inhibit subclinical pathogenic bacterial infections, increase uptake and utilization of nutrients through the intestinal wall, and suppress the activity and population of bacteria in the intestines and thus, preserve the energy in feed that would be lost due to microbial fermentation, promoting animal growth through nutrient and energy availability enhancement (Gaskins et al. 2002). Registered animal antibiotics for use as growth promoter/feed efficiency in Australia, Denmark, European Union (EU), and Canada are well summarized in Sarmah et al. (2006). The antibiotics approved for use in U.S. food-producing animals are given in Table 2.1. Relative usage of these chemicals is illustrated in Fig. 2.1.

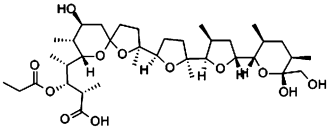
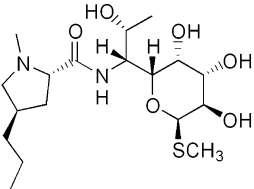
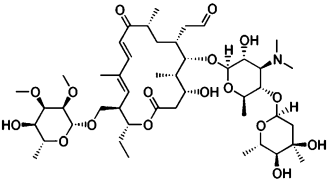
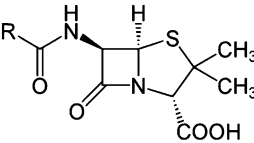
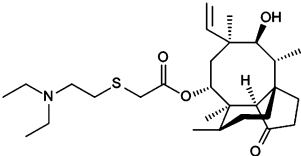
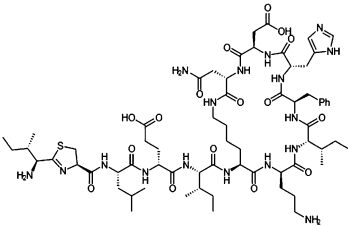

Addition of antibiotics to animal feed is recommended at dose ranging from 3 to 220 mg kg⁻¹, depending on the species and growth stage of the animal and the type of antibiotics (McEwen and Fedorka-Cray 2002). Multiple antibiotics are often supplemented in combination. Some antibiotics are added for a specific growth stage of animals but some could be fed continuously up to the point of slaughter (Kumar et al. 2005a). Furtula et al. (2009) reported that chicken feeds in British Columbia, Canada contained multiple antibiotics at concentrations varying with bird growth phases, typically 22 mg kg⁻¹ virginiamycin, 99 mg kg⁻¹ monensin, 120 mg kg⁻¹ salinomycin, 80 mg kg⁻¹ narasin, 80 mg kg⁻¹ nicarbazin, 165 mg kg⁻¹

Table 2.1 Antimicrobials drugs approved for use in food-producing animals in the U.S.

Antimicrobial class	Basic chemical structure	Individual drugs
Aminocoumarins		Novobiocin
Aminoglycosides		Apramycin ^a Dihydrostreptomycin Efrotomycin Gentamicin Hygromycin B Neomycin ^a Spectinomycin Streptomycin
Amphenicols		Florfenicol
Cephalosporins		Ceftiofur Cephapirin
Diaminopyrimidines		Ormetoprim
Fluoroquinolones		Danofloxacin Enrofloxacin
Glycolipids		Bambermycin ^a

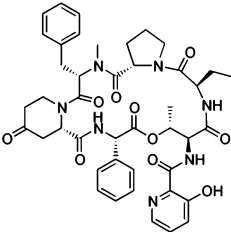
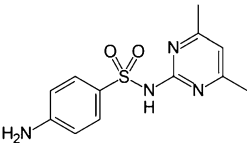
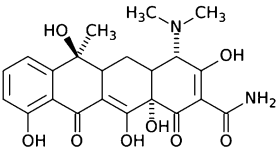
(continued)

Table 2.1 (continued)

Antimicrobial class	Basic chemical structure	Individual drugs
Ionophores		Laidlomycin Lasalocid Monensin Narasin Salinomycin Semduramicin
Lincosamides		Lincomycin ^a Pirlimycin
Macrolides		Carbomycin Erythromycin Oleandomycin Tilmicosin Tulathromycin Tylosin ^a
Penicillins		Amoxicillin Ampicillin Cloxacillin Hetacillin Penicillin ^a
Pleuromutilins		Tiamulin ^a
Polypeptides		Bacitracin ^a Polymixin B
Quinoxalines		Carbadox ^a

(continued)

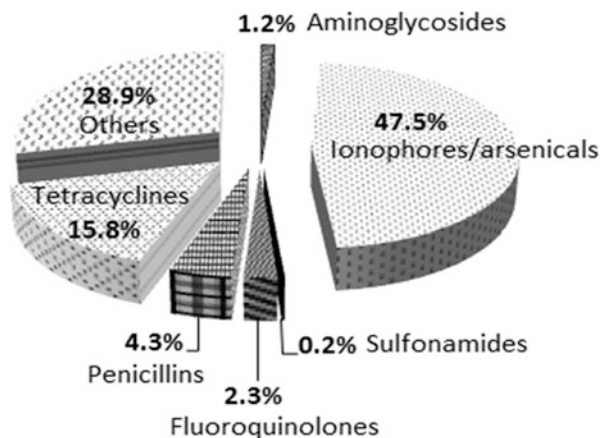
Table 2.1 (continued)

Antimicrobial class	Basic chemical structure	Individual drugs
Streptogramins		Virginiamycin ^a
Sulfas		Sulfachlorpyridazine Sulfadimethoxine Sulfamerazine Sulfamethazine ^a Sulfaquinoxaline Sulfathiazole ^a
Tetracyclines		Chlortetracycline ^a Oxytetracycline ^a Tetracycline

Source: FDA (2010)

^aApproved for use as **swine** feed supplements for therapeutic purposes (carbadox, sulfamethazine, and sulfathiazole) and for promoting pig growth (others)

Fig. 2.1 Relative percentages of the used antibiotics for animal production in the US in 1999 (Source: Sarmah et al. 2006)



bacitracin, and 22 mg kg⁻¹ penicillin in empirical combinations. Currently the U.S. Food and Drug Administration (FDA) approves 14 antibiotics for use in swine feed (Table 2.1), of which 11 are recommended as growth promoters at 2–150 mg kg⁻¹ of feed (Holt 2008). Due to the development of bacterial antibiotic resistance, however, animal feeds often contain antibiotics at contents higher than the recommended

levels. A survey revealed that 25 % of the 3,000 tested swine feeds in the U.S. contained antibiotics at higher-than-the-recommended concentrations (Dewey et al. 1997). The widespread use of antibiotics at increasing rates may facilitate the evolution of bacteria toward antibiotics-resistant strains and consequently, induce new, untreatable livestock diseases (Kumar et al. 2005a). Antibiotics inhibit or destroy sensitive bacteria, providing an environment for those resistant variants to flourish and become dominant. The antibiotic resistance can be further transferred via plasmids to other bacteria.

Globally it is unclear what veterinary pharmaceuticals and in what quantities are being used, as data on the annual production and consumption of animal medicines are not readily available in many countries. The U.S. uses 13,067 tons of veterinary antibiotics in domestic animal agriculture and exports 1,632 tons to other countries annually (FDA 2010). In China, more than 6,000 tons of veterinary antibiotics are consumed annually (Zhao et al. 2010); the most common antibiotics are tetracyclines, sulfonamides, tylosin, and fluoroquinolones (Li et al. 2013). In the United Kingdom, 897 tons of antibiotics were applied to animal production in 2000 (Thiele-Bruhn and Aust 2004). The annual EU consumption of veterinary antibiotics was approximately 5,000 tons by 2005 (Kumar et al. 2005a). Since 2006, the use of antibiotics as a feed supplement of food-producing animals has been banned in EU countries (Europa 2005).

2.3 Residual Veterinary Pharmaceuticals in Animal Manures

The use of veterinary pharmaceuticals is vitally important in confined food animal production. Nevertheless, animals do not utilize all the applied pharmaceuticals. Depending on the chemical and the animal species, 10–90 % of the feed-supplemented pharmaceuticals are excreted in animal urine and feces as intact parent compounds or bioactive metabolites (Kumar et al. 2005a). Through controlled-feeding trials with broilers eating antibiotics-supplemented feeds for 36 days, Kumar et al. (2004) found that 3–60 % of the antibiotics penicillin, salinomycin, bacitracin, chlortetracycline, virginiamycin I, virginiamycin II, monensin, and narasin added separately or in combination at 2–110 mg kg⁻¹ in feed were excreted in bird manure. With the advances of analytical techniques, antibiotics such as tetracyclines, tylosin, monensin, sulfadimidine, and sulfathiazole have been detected in swine slurry, cattle manure, poultry litter, and fish farm sediment from different countries at a wide concentration range from trace to 200 mg kg⁻¹ or mg L⁻¹ (Kumar et al. 2005a). Literature reported concentrations of residual veterinary pharmaceuticals in manure wastes from confined food-producing animals are summarized in Table 2.2.

Detection of residual veterinary pharmaceuticals in manures is typically achieved by extracting animal waste with nonpolar and polar solvent extractants, purifying

Table 2.2 Reported concentrations of residual veterinary pharmaceuticals in animal manures

Manure type	Pharmaceuticals	Concentration	Country	References
Swine manure	Sulfonamides	0.01–29 mg kg ⁻¹	China	Pan et al. (2011)
	Tetracyclines	0.03–765 mg kg ⁻¹		
	Macrolide	0.05–0.11 mg kg ⁻¹		
Swine manure	Tetracyclines	0.3–56.8 mg kg ⁻¹	China	Li et al. (2013)
	Sulfas	0.1–4.8 mg kg ⁻¹		
	Tylosin	0.2–1.9 mg kg ⁻¹		
	Sulfamethazine	3.3–8.7 mg kg ⁻¹		
Manure from mother pigs with farrows	Sulfathiazole	0–12.4 mg kg ⁻¹	Switzerland	Haller et al. (2002)
	Trimethoprim	Traces		
Manure from fattening pigs	Sulfamethazine	0.13–0.23 mg kg ⁻¹	Switzerland	Haller et al. (2002)
	Sulfathiazole	0.10–0.17 mg kg ⁻¹		
	Tetracyclines	0.1–46 mg kg ⁻¹		
Swine slurry	Sulfadimidine	0.1–20 mg kg ⁻¹	Australia	Carballo et al. (2007)
	Tetracycline	14–41 mg kg ⁻¹		
Swine slurry	Sulfamethazine	0–7.2 mg kg ⁻¹	Germany	Hamscher et al. (2005)
	Sulfadiazine	3.5–11.3 mg kg ⁻¹		
Swine slurry	Tetracycline	0.04–0.70 mg L ⁻¹	Denmark	Seingeløv et al. (2003)
	Chlortetracycline	0.068–1.0 mg L ⁻¹		
Swine lagoon slurry	Tetracycline	0.025–0.41 mg L ⁻¹	USA	Campagnolo et al. (2002)
	Sulfamethazine	0.1–0.4 mg L ⁻¹		
Swine manure lot liquid	Lincomycin	0.07–0.24 mg L ⁻¹	USA	Kumar et al. (2004)
	Chlortetracycline	3.5–5.2 mg L ⁻¹		
	Tylosin	3.3–7.9 mg L ⁻¹		
Swine manure lot liquid	Tetracycline	3.2–4.0 mg L ⁻¹	Germany	Hamscher et al. (2002)
	Chlortetracycline	0.09–0.10 mg L ⁻¹		
Poultry litter	Salinomycin	0.32–4.4 mg kg ⁻¹	Canada	Furtula et al. (2010)
	Bacitracin	0.01–1.76 mg kg ⁻¹		
	Narasin	2.2–33.0 mg kg ⁻¹		
	Nicarbacin	5.4–22.4 mg kg ⁻¹		

Poultry manure ^a	Tetracyclines Sulfas Tylosin	0.5–13.4 mg kg ⁻¹ 0.1–7.1 mg kg ⁻¹ 0.2–0.4 mg kg ⁻¹	China	Li et al. (2013)
Poultry manure ^a	Tetracyclines Sulfas	0.05–0.5 mg kg ⁻¹ 3–37 mg kg ⁻¹	Turkey	Karci and Balcioglu (2009)
Poultry manure ^a	Enrofloxacin	0.01–0.08 mg kg ⁻¹	Canada	Warman and Thomas (1981)
Broiler manure ^a	Chlortetracycline Tetracyclines	23 mg kg ⁻¹ 0.1–1.7 mg kg ⁻¹	Australia	Carballo et al. (2007)
Turkey manure ^a	Sulfadiazine Enrofloxacin	3.1–5.1 mg kg ⁻¹ 0.2–2.8 mg kg ⁻¹	Australia	Carballo et al. (2007)
Dairy cow manure ^a	Sulfadiazine Enrofloxacin Tetracyclines	3.1–9.1 mg kg ⁻¹ 0.2–8.3 mg kg ⁻¹ 0.2–10.4 mg kg ⁻¹	China	Li et al. (2013)
Beef cattle manure ^a	Sulfas Tylosin Chlortetracycline	0.1–1.0 mg kg ⁻¹ 0.2–0.3 mg kg ⁻¹ 5.3 mg kg ⁻¹	USA	Patten et al. (1980)
Cattle manure ^a	Oxytetracycline	11.3 mg kg ⁻¹	Canada	Donoho (1984)
Fresh cattle manure ^a	Monensin Oxytetracycline	1–5 mg kg ⁻¹ 872 mg kg ⁻¹	Italy	De Liguoro et al. (2003)
Newly removed cattle bedding	Tylosin Oxytetracycline	116 mg kg ⁻¹ 367 mg kg ⁻¹	Italy	De Liguoro et al. (2003)
Mixed swine and cattle slurries	Tylosin Sulfas	32.8 mg kg ⁻¹ 20 mg kg ⁻¹	Switzerland	Haller et al. (2002)
Aged cattle manure and bedding mixture	Sulfamethazine Tetracyclines	0.13–8.7 mg kg ⁻¹ 0.05–0.4 mg kg ⁻¹	Turkey	Karci and Balcioglu (2009)
	Sulfas	0.1–8 mg kg ⁻¹		

^aManure is equivalent to feces

and concentrating the extracts using solid phase extraction (SPE) columns, and determining the processed extracts for concentrations of target chemicals using liquid chromatography-mass spectrometry (LC-MS) or high performance liquid chromatography (HPLC) techniques, with chemical standards for calibration. Due to low extraction efficiency and poor recovery of pharmaceuticals from background-complex waste media, accurate measurement of residual veterinary drugs in animal waste is always challenging. Extractants consisting of weakly acidic buffers and organic solvents (e.g., 1:1 methanol: pH 4.0 EDTA-McIlvaine buffer) are recommended to recover residual antibiotics from lyophilized manure materials (Thiele-Bruhn 2003). For certain veterinary chemicals, other formulated extractants (e.g., deionized water, a methanol-water mixture, or pure methanol) may be more efficient (Michellini et al. 2012). Methods such as repeated extraction, accelerated solvent extraction (ASE), ultrasonic liquid extraction, and Soxhlet extraction are commonly used to improve the extraction efficiency. Experiments with artificial antibiotic spiking disclosed 64–107 % efficiency of extracting pharmaceutical from manures (Furtula et al. 2009; Li et al. 2013). As instantaneous chemical spiking does not incorporate the “aging effect” of antibiotic-manure matrix interactions (i.e., chemicals being more tightly sorbed in the media and over time becoming more difficult to extract), the measured recovery rates may have over-estimated the actual extraction efficiency from genuine samples.

Most veterinary pharmaceuticals are biodegradable and therefore, storage or composting of animal manure helps eliminate the residual chemicals (Dolliver et al. 2008). De Liguoro et al. (2003) reported that the concentrations of oxytetracycline and tylosin in cattle manure decreased from 366.8 to 2.1 mg kg⁻¹ and from 32.8 to <0.1 mg kg⁻¹, respectively, after heaping the waste outdoor for 135 days. Degradation of veterinary pharmaceuticals in animal manures is chiefly a result of microbial activity. As a result, manure sterilization significantly inhibited degradation of the residual veterinary chemicals (Wang et al. 2006). Degradation of veterinary pharmaceuticals in animal manures by the inherent microorganisms poses challenges for accurately measuring the residual level of animal drugs in excreta. Meanwhile it suggests an effective approach for reducing bioactive chemical contamination simply by stockpiling or composting animal waste for adequate time (e.g., 2–3 months) prior to land disposal.

2.4 Environmental Behaviors of Veterinary Pharmaceuticals in Soils

Veterinary pharmaceuticals are introduced into the environment through discharge, handling, storage, and disposal of animal waste. Antibiotics in excreta from grazing livestock and in water of aquaculture ponds reach the environment by direct discharge. Collected manures (in storage sheds, slurry tanks, and lagoons) and processed products (e.g., compost, sewage sludge) are commonly applied via

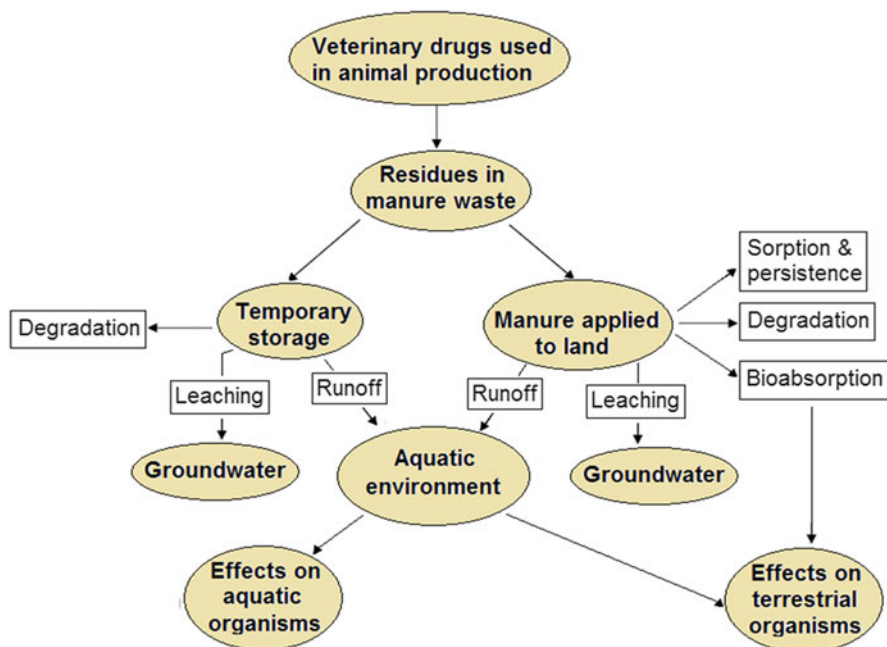


Fig. 2.2 Expected fate, transport, and exposure pathways for veterinary pharmaceuticals in the environment

spreading, injection, or irrigation to cropland as an organic fertilizer. In the U.S., the food animal industry generates annually 8.5 million dry tons of swine manure, 16.2 million dry tons of poultry litter, and 107.4 million dry tons of cattle waste, of which the vast majority is disposed of through land application (Kumar et al. 2005a). If assume 50 % (in the range of 10–90 %) of the 13,067 tons of veterinary antibiotics consumed annually (FDA 2010) are excreted in animal waste, there were more than 6,500 tons of drug chemicals entering the U.S. soil and water environments.

Anticipated transport and exposure pathways of animal waste-derived veterinary pharmaceuticals are outlined in Fig. 2.2. In soil, veterinary pharmaceuticals may be adsorbed by soil solids, degraded by soil microorganisms, taken up by plants, transport to surface water via runoff and to groundwater via leaching, and generate adverse impacts on terrestrial and aquatic ecosystems.

2.4.1 Sorption of Veterinary Pharmaceuticals in Soils

In soils, veterinary pharmaceuticals interact with clay minerals and organic matter, resulting in sorption, binding, and fixation of the chemicals in the soil matrix. The strength of the interaction is dependent on the chemical species and the soil

Table 2.3 Water solubility and soil distribution coefficient of veterinary pharmaceuticals

Drug class	Antibiotics	Water solubility (mg L ⁻¹)	K _d (L kg ⁻¹)	K _{OC} (L kg ⁻¹)
Tetracyclines	Tetracycline	230–52,000	420–1,030	27,800–93,300
	Chlortetracycline			
	Oxytetracycline			
Sulfonamides	Sulfanilamide	7.5–00	0.6–4.9	60–200
	Sulfadiazine			
	Sulfadimidine			
	Sulfadimethoxine			
	Sulfapyridine			
	Sulfamethoxazole			
Aminoglycosides	Efrotomycin	10–500	8–290	580–11,000
	Kanamycin			
	Neomycin			
	Streptomycin			
β-lactams	Ampicillin	22–10,100	NA	NA
	Meropenem			
	Penicillin G			
	Ceftiofur			
	Cefotiam			
Macrolides	Erythromycin	0.45–15	8.3–128	770–7,990
	Oleandomycin			
Fluorquinolones	Tylosin	3.2–17,790	260–6,310	16,500–770,000
	Ciprofloxacin			
	Enrofloxacin			
	Flumequin			
	Sarafloxacin			
Imidazoles	Oxolinic acid	6.3–407	0.54–0.67	38–56
	Fenbendazole			
	Metronidazole			
	Oxfendazole			
Polypeptides	Avermectin	Insoluble – miscible	18–134	4,760–6,600
	Bacitracin			
	Ivermectin			
	Virginiamycin			
Polyethers	Lasalocid	<0.003	1–210	61–15,700
	Monensin			
	Salinomycin			
Glycopeptides	Vancomycin	>1,000	0.3–0.7	NA
Quinoxalines	Olaquinox	1,000,000	0.69–1.67	46–116

Source: Yeager and Halley (1990), Tolls (2001), Thiele-Bruhn (2003), Sassman and Lee (2007)

property and is influenced by temperature, moisture, and the soil solution chemistry (Kumar et al. 2005a). A parameter “distribution (partition) coefficient” K_d (the ratio of the quantity of an adsorbate sorbed per unit mass of sorbent solid to the amount of the adsorbate remaining in solution at equilibrium; normally predicted from the linear portion of the adsorption isotherms) is commonly used to measure the

sorption of a solute to soil. It is believed that sorption of organic contaminants in soil is mainly via interactions with soil organic matter (SOM) and thus, the adsorption coefficient K_{OC} (K_d normalized by soil organic carbon (OC) content f_{OC} : $K_{OC} = K_d/f_{OC}$) also serves as a measure of sorption (Kishi et al. 1990). Veterinary chemicals with increased aromaticity and electropolarity demonstrate higher K_d and K_{OC} values and tend to be strongly bound to soils (Thiele-Bruhn et al. 2004). The K_d and K_{OC} values of selected veterinary pharmaceuticals are given in Table 2.3.

Sorption of veterinary pharmaceuticals to soil constituents occurs naturally and ubiquitously, especially for those with high K_d or K_{OC} values (Table 2.3). The sorption is generally rapid: in antibiotics-spiked (400–12,000 mg kg⁻¹) soil slurry systems under agitation, more than 95 % of the chlortetracycline adsorption to a sandy loam and a clay soil occurred within 10 min and 95 % of the tylosin adsorption occurred within 3 h (Allaire et al. 2006). Soil active sorption sites include SOM and the broken edges, basal planes, and interlayer space of clay minerals (Nowara et al. 1997). For compounds with significant hydrophobic moieties (i.e., compounds with high octanol/water partition coefficients), sorption to soil is mainly via hydrophobic partitioning into SOM. Gruber et al. (1990) found that sorption of avermectin B1a to three different textured soils increased as the SOM increased and the K_d showed an evidently positive relationship with f_{OC} , suggesting predominance of hydrophobic partitioning in this particular antibiotic sorption. By studying migration of carbamazepine, naproxen and diclofenac in field soil profiles with artificial irrigation, Chefetz et al. (2008) concluded that sorption of the pharmaceuticals to soil was governed by SOM in its quantity and physiochemical nature. For hydrophilic, ionizable antibiotics, however, hydrophobic partitioning may not be dominant. Instead, physiochemical interactions with soil minerals become more important. A review by Tolls (2001) noticed that the K_d values of animal antibiotics varied greatly with soil types, but translation to K_{OC} by normalizing the values with soil f_{OC} did not significantly decrease the variation, suggesting clay minerals were also important in binding veterinary pharmaceuticals. The binding mechanisms include van der Waals interaction, electrostatic attraction, cation bridging, and anion exchange. Studies showed that sorption of tetracycline, oxytetracycline, oxolinic acid, and enrofloxacin to pure clay minerals and sediments increased with increasing the sorbent surface area (Sithole and Guy 1987; Nowara et al. 1997), indicating a surface-related process of antibiotics to soil. Many pharmaceuticals contain functional groups such as amines, carboxyls, and hydroxyls (Table 2.1). Protonation or deprotonation of these groups in pH-specific media engenders positive or negative charges. Positively-charged antibiotics bind to soil particles through electrostatic attraction/cation exchange (Gao and Pedersen 2005; Wang et al. 2012). Anionic pharmaceutical molecules form complexes with cations that are adsorbed on negatively charged soil constituents; the cation bridging enables the pharmaceuticals to be retained in soils (Tolls 2001). In alkaline solutions, some antibiotics can even form complexes with clay minerals through anion exchange whereby the carboxylic groups of the chemicals directly replace the hydroxyl groups on mineral surfaces. This type of sorption is so strong that a phosphate solution is required to extract the sorbed antibiotics (Sassman and Lee 2007).

Furthermore, sorption of antibiotics to soil minerals is affected by the media pH, ionic strength, and types of exchangeable cations (Pils and Laird 2007; Wang et al. 2012). The media pH influences drug-soil interactions by altering the charges of pharmaceuticals and the cation exchange capacity (CEC) of soils. For example, at pH 5.0 oxytetracycline has zero charges and interacts with organic matter mainly via hydrophobic partitioning; at lower and higher pH, the chemical becomes positively and negatively charged, respectively, and was sorbed to soil minerals mainly via cation exchange and cation bridging, respectively (Kulshrestha et al. 2004). Sassman and Lee (2005, 2007) noticed that the CEC-normalized sorption of tetracyclines and the f_{OC} -normalized sorption of monensin and lasalocid to soils decreased with increasing soil pH in the range of 4.2–7.5. Wang et al. (2008) observed that the presence of Cu^{2+} enhanced sorption of tetracycline to montmorillonite in a wide pH range. Similar to clay minerals, SOM contains various functional groups and is typically negatively charged. Polar pharmaceutical compounds are also sorbed to soil through interactions with SOM via van der Waals force, electric attraction, cation bridging, and anion exchange (MacKay and Canterbury 2005; Gu et al. 2007; Sibley and Pedersen 2008). Agricultural soils are typically low in OC content (i.e., $f_{OC} < 3\%$) and therefore, these types of interaction may not be as contributing as with soil minerals.

Considering that most veterinary pharmaceuticals consist of both hydrophobic and hydrophilic moieties (Table 2.1), it can be concluded that sorption of veterinary pharmaceuticals in soils is a result of interactions of the chemicals with soil clay minerals and SOM chiefly through hydrophobic partitioning, electric attraction, and cation bridging. The interactions are determined by the physiochemical nature of the pharmaceuticals and the soils (e.g., the quantity and the type of soil clay and SOM) and are impacted by the soil solution chemistry. As such, Jones et al. (2005) identified soil texture, CEC, and iron oxide content as the most important factors that determined the K_d values of oxytetracycline in 26 $OC < 4\%$ soils. Sorption of sulfamethazines in five different mineral soils was influenced by soil OC content, soil surface area, and soil solution pH (Lertpaitoonpan et al. 2009).

2.4.2 Transport of Veterinary Pharmaceuticals in Soil

Once in soil through land application of animal waste, residual veterinary pharmaceuticals can be transported from the manure-applied fields to groundwater through percolation (leaching) and to surface waters through runoff. The chemicals weakly bound to soil materials (small K_d , Table 2.3) are likely to migrate out of the field in runoff water or be leached down in the soil profile by percolation water, whereas those strongly sorbed by soil solids (high K_d , Table 2.3) can move to other locations together with associated soil particles eroded by runoff water (Davis et al. 2006; Kim et al. 2010; Chen et al. 2011). The mobility of antibiotic chemicals in soils is controlled by their sorptivity and life time and influenced by soil solution pH and ionic strength (Rabølle and Spliid 2000; Blackwell et al. 2007; Chen et al. 2011).

Furthermore, sorptive veterinary pharmaceuticals can form associations with colloids and dissolved organic matter (DOM) and migrate readily in the soil profile through preferential flow channels (Zitnick et al. 2011; Ding et al. 2013; Zou and Zheng 2013).

To reduce runoff losses of veterinary chemicals, immediate soil incorporation of land applied animal waste becomes important (Boxall 2008). Runoff losses of antibiotics (e.g., sulfonamides) could be one to two orders of magnitude higher from grassland than from cultivated land receiving surface application of manure slurry (Kreuzig et al. 2005). Moreover, surface applied manure can significantly increase the amount of runoff water from the treated field, likely due to the surface sealing effect of manure particulates (Burkhardt et al. 2005). Surface runoff of veterinary pharmaceuticals from animal waste has spread the chemicals to the general water environment. Lissimore et al. (2006) surveyed seven tributaries of an agricultural watershed in Southern Ontario, Canada for occurrence of veterinary pharmaceuticals in surface water and detected 14 antibiotics in 125 stream samples, with prevalence of lincomycin, monensin, carbamazepine, and sulfamethazine at median concentrations by 44 ng L^{-1} . In Lansing (Michigan, USA) where animal manures from confined livestock feeding operations were extensively applied to cropland, antibiotics were detected in waters from 11 farm drainage tile channels and surface ditches, with amprolium by 288 ng L^{-1} and monensin by 189 ng L^{-1} at approximately 50 % detection frequency of 109 samples (Song et al. 2010).

2.4.3 Transformation of Veterinary Pharmaceuticals in Soils

In agricultural soils, residual veterinary pharmaceuticals introduced by land application of animal manure are subject to abiotic and biotic transformation and degradation. The degradability and degradation pathways vary significantly with veterinary chemicals and the transformation rate is influenced by a number of environmental factors including soil type, soil conditions (temperature, moisture, and oxygen status), manure type, soil-manure ratio, pH, and light (Boxall 2008; Lin and Gan 2011). Reported studies on degradation of veterinary pharmaceuticals in soils are summarized in Table 2.4.

Under general conditions, most animal antibiotics are degradable in soil, especially in the presence of manure waste, with a half-life time <30 days. Certain antibiotics such as roxithromycin, sarafloxacin, and virginiamycin, however, can be persistent and remain largely unchanged in soil over 120 days (Table 2.4). Degradation of veterinary pharmaceuticals in agricultural soils is a comprehensive result of microbial decomposition, organic transformation, oxidation, photolysis, and hydrolysis. Chee-Sanford et al. (2009) reviewed the possible degradation pathways of manure-introduced antibiotics in soil. As water is always present in animal waste and natural soils, hydrolysis may be an important mechanism for animal pharmaceuticals to dissipate in the environment. It is known that the antibiotics β -lactams, macrolides, and sulfonamides are susceptible to hydrolysis

Table 2.4 Reported studies on degradation of veterinary pharmaceuticals in soils

Pharmaceuticals	Methods/degradation conditions	Degraded, (%)	Half life $t_{1/2}$ (day)	References
Ceftiofur sodium	Three agricultural soils (70 % moisture capacity) were fortified with ceftiofur sodium at 10 mg C/50 g soil and incubated at 22 °C for 7 weeks	49–79	22–49	Gilbertson et al. (1990)
Bambermycin	Spiked individual antibiotics to chicken feces-amended soils at 5.6 mg kg ⁻¹ and incubated the mixtures for 30 days at 30 °C, 20 °C, and 4 °C, respectively	100, 100, 10		Gavalchin and Katz (1994)
Barcitracin		71, 67, 77		
Chlortetracycline		56, 12, 0		
Erythromycin		100, 75, 3		
Tylosin		100, 100, 60 ^a		
Sarafloxacin	Fortified three agricultural soils (50–70 % field capacity with sarafloxacin at 3.4 mg kg ⁻¹) and incubated the soils at 22 °C in the dark for 80 days	0.5–0.6 %	Persistent	Marengo et al. (1997)
Virginiamycin	Incubated [14C] virginiamycin at 0.5 mg C/50 g soil with six agricultural soils (pH 5.4–8.2, clay 5–33 %, 50–70 % of field capacity) that were amended with glucose at 9.5 mg C/50 g soil at room temperature for 64 days with daily air flushing	12–40	87–173	Weerasinghe and Towner (1997)
Sulfadimethoxine	A 20 % moisture silt loam was amended with sulfadimethoxine-fortified steer manure and incubated at 25 °C for 70 days	89	3–11	Wang et al. (2006)
Erythromycin	Spiked a 12 % moisture sandy loam with combined six antibiotics each at 2 mg kg ⁻¹ and incubated the soil at 20 °C in the dark for 120 days	98	20	Schlüsener and Bester (2006)
Oleandomycin		95	27	
Roxithromycin		25	Persistent	
Salinomycin		100	5	
Tiamulin		99	16	
Tylosin		100	8	
Sulfamethazine		70–83	19	
Sulfachloropyridine	Applied sulfonamides to two moist soils at by 100 mg kg ⁻¹ and incubated the soils at 25 °C in the dark for 40 days	61–66	21	

(continued)

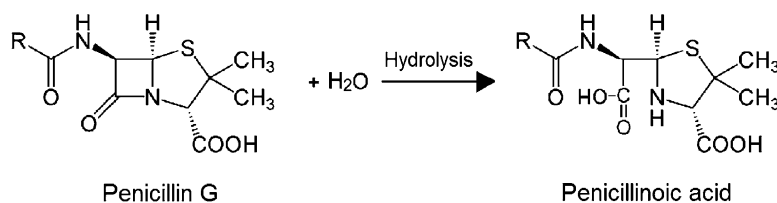
Table 2.4 (continued)

Pharmaceuticals	Methods/degradation conditions	Degraded, (%)	Half life $t_{1/2}$ (day)	References
Oxytetracycline	200 L of liquid swine manure were fortified with 7.08 g oxytetracycline and 5.24 g sulfachloropyridine and surface applied to a 120-m ² sandy loam field plot. 127 days	83	21–23	Blackwell et al. (2007)
Sulfachloropyridine		98	3–4	
Tylosin	Incubated 50 mg kg ⁻¹ tylosin-spiked sandy loam (field capacity) at 20 °C in the dark for 30 days	93	7–8	Hu and Coats (2007)
Monensin	Spiked two contrasting soils (field capacity) with separately monensin and lasalocid at 2 mg kg ⁻¹ and incubated the soils at 23 °C in the dark for 30 days	100	1.2–1.9	Sassman and Lee (2007)
Lasalocid		99	1.4–3.6	
Diclofenac ^b	Spiked a sandy and a loamy moist soil with the compounds each at 40 µg kg ⁻¹ and incubated the soils at 21 °C in dark	92–100	4.8–29.6	Lin and Gan (2011)
Ibuprofen ^b		96–100	10.4–15.2	
Naproxen ^b	under aerobic conditions for 84 days	59–97	17.4–84.8	
Sulfamethoxazole ^b		90–95	9.0–11.4	

^aDegraded at 30, 20, and 4 °C, respectively

^bHuman medicines. Not used for animal treatments

(Huang et al. 2001). Under mild acidic or basic conditions, penicillin G can be readily transformed to penicillinoic acid through hydrolysis (Huang et al. 2001):



If exposed to daylight, antibiotics may undergo photolysis at the soil-atmosphere interface. Quinolones and tetracyclines are particularly sensitive to photo irradiation

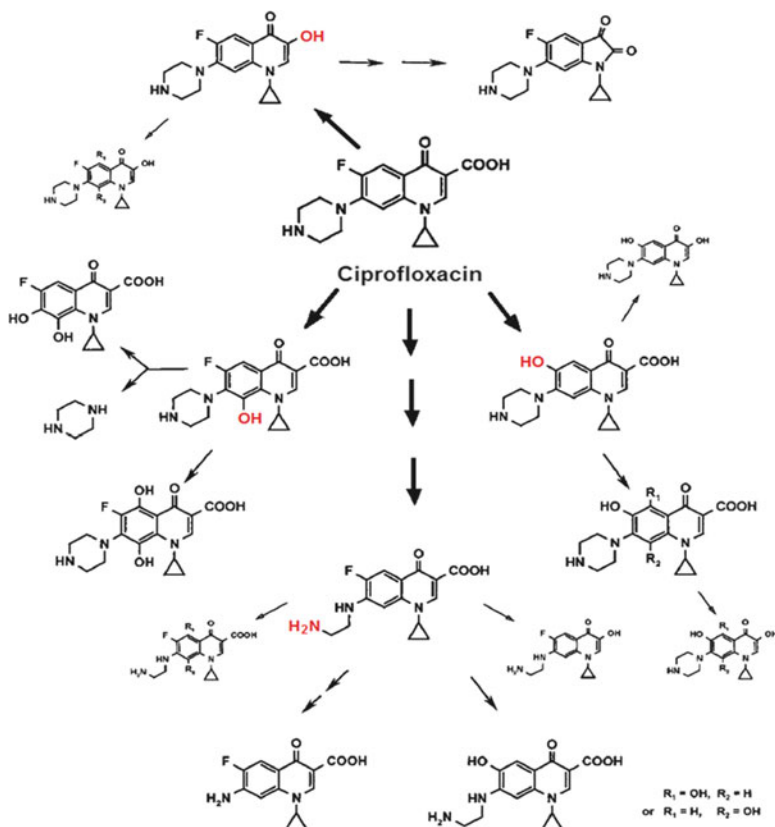
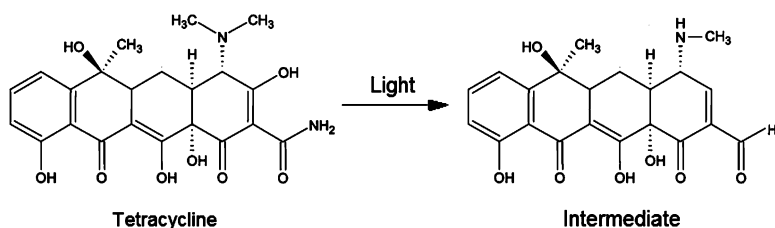


Fig. 2.3 Proposed pathways for the microbial degradation of ciprofloxacin by the fungus *G. striatum* in cultural solutions. Primary hydroxylation at one of the several alternative sites initiates four principal degradation routes. Metabolites identified by HPLC-MS are included at reduced size (Source: Wetzstein et al. 1999)

(Doi and Stoskopf 2000). The photolysis reaction of tetracycline in water under light can be described as (Jiao et al. 2008):



Compared to other reactions, however, photodegradation of antibiotics may be minor under field conditions due to limited light exposure (Beausse 2004). Instead,

biodegradation is the major pathway for antibiotics transformation in soil. Many veterinary chemicals are susceptible to enzymatic degradation reactions such as oxidative decarboxylation and hydroxylation (Al-Ahmad et al. 1999). Hydroxylation of the antibiotic ciprofloxacin initiated by the fungus *G. striatum* in a cultural solution lead to further biodegradation of the chemical to a number of metabolites (Fig. 2.3). Microbial addition by inoculating surface water with activated sewage sludge, recycled beef farm water, or lake sediments resulted in significantly accelerated degradation of the inherent veterinary antibiotics (Gartiser et al. 2007; Li et al. 2011), whereas microbial depletion by sterilizing agricultural soils greatly inhibited degradation of various antibiotic chemicals (Accinelli et al. 2007; Lin and Gan 2011).

In addition to biodegradation, chemical processes other than hydrolysis and photolysis are also important for antibiotic transformation in soil. Soil organic matter possesses a variety of functional groups such as amines, carboxyls, carbonyls, ethers, hydroxyls, nitriles, nitrosos, sulfides, and sulfonyls (Swift 1996) and is active in reacting with veterinary chemicals. Hu and Coats (2007) found that in autoclaved soils (OC 1.6 %), tylosin degraded rapidly and demonstrated a half-life of 8 days. Hydrolysis or photolysis could not explain the rapid degradation, as in irradiated water tylosin showed a half-life of 200 days. The same authors also noticed that tylosin degraded in nonsterilized soils at a rate nearly equal to that in the sterilized soils. This does not indicate that biodegradation of tylosin was insignificant. Likely, the spiked antibiotic at 50 mg kg^{-1} soil had inhibited the microbial activity, creating an equivalently sterile environment. The inhibitory effect of antibiotics on the resident microorganisms has been noticed (Gartiser et al. 2007).

Temperature influences degradation of veterinary pharmaceuticals in soils. Gavalchin and Katz (1994) spiked chlortetracycline and erythromycin to chicken feces-amended soils at 5.6 mg kg^{-1} and incubated the soils at different temperatures. After 30 days of 30, 20, and 4°C incubation, 56 %, 12 %, and 0 % of the spiked chlortetracycline dissipated, respectively and for erythromycin, the levels were 100 %, 75 %, and 3 %, respectively. Li et al. (2011) observed that ceftiofur hydrolyzed to desfuroylceftiofur in deionized water, with a half-life time of 289 days at 15°C . The half-life time was shortened to 96, 21, and 5 days, respectively, as the hydrolysis temperature increased to 25, 35, and 45°C . Degradation of veterinary pharmaceuticals is also influenced by soil oxygen availability. Dissipation of diclofenac, ibuprofen, naproxen, sulfamethoxazole, and trimethoprim from two mineral soils under anaerobic conditions was substantially slower than under aerobic conditions (Lin and Gan 2011). Sorption to soil minerals and SOM preserves veterinary antibiotics and enhances their persistence in soils (Zitnick et al. 2011). Smith et al. (1992) reported that microbial utilization of [14C] quinoline from solution was 30 times more rapid than from the bound on surfaces of suspended clay particles. A higher soil moisture content allows more chemicals in the solution phase, enhancing the accessibility to microorganisms. Wang et al. (2006) reported that the half-life time of sulfadimethoxine in a silt loam decreased from 10.4 days to 6.9 days and further to 4.9 days as the soil moisture content was elevated from 15 % to 20 % and additionally to 25 %, respectively. Degradation of veterinary

pharmaceuticals is further influenced by soil pH. For example, the half-life time of virginiamycin in different agricultural soils ranged from 87 to 173 days and was negatively correlated to soil pH (Weerasinghe and Towner 1997). In neutral or alkaline solutions, tylosin hydrolyzed to tylosin aldol; at pH <4, however, the main hydrolysis product became desmycosin (Paesen et al. 1995). As organic matter and microorganisms promote antibiotic degradation, amendment of soil with more animal manure typically accelerate the dissipation of veterinary pharmaceuticals (Wang et al. 2006). Clearly, many environmental factors influence the stability and persistence of animal pharmaceuticals in soils and subsequently, affect their transport and potential ecological impacts in agricultural systems.

2.4.4 Uptake and Accumulation of Veterinary Pharmaceuticals in Crop Plants

In soil, residual veterinary pharmaceuticals can be absorbed by plants and accumulated in soil fauna. The uptake and accumulation, however, may vary with organism species and pharmaceutical compounds. Bioaccumulation of antibiotics by plants has been confirmed using *in-vitro* laboratory research. The plants millet (*Panicum miliaceum*), maize (*Zea mays*), and pea (*Pisum sativum*) grown in a culture medium containing 300 mg L⁻¹ sulfadimethoxine for 8–18 days showed concentrations of the antibiotic ranging from 178 to 2,070 mg kg⁻¹ in their roots and 12.5–110 mg kg⁻¹ in their stalk/leaves (Migliore et al. 1995). In a greenhouse trial, barley (*Hordeum distichum* L.) grown in soils spiked with sulfadimethoxine at 109 mg kg⁻¹ for 45 days accumulated the antibiotic 79.0 mg kg⁻¹ in its roots and 18.2 mg kg⁻¹ in its leaves (Migliore et al. 1996). Corn, cabbage, and green onion grown in swine manure-amended soil pots containing chlortetracycline and tylosin each at 0.58–1.58 mg kg⁻¹ soil for 3–6 weeks accumulated chlortetracycline in plant tissues at 2–17 µg kg⁻¹ fresh weight but not tylosin (Kumar et al. 2005b). Bioaccumulation of sulfamethazine by corn, lettuce, and potato from swine slurry-fertilized, 1.25–2.50 mg kg⁻¹ sulfamethazine-fortified potting soils ranged from 0.1–1.2 mg kg⁻¹ dry weight in above-ground plant tissues (Dolliver et al. 2007). Willow and maize grown in greenhouse potting soils spiked with 10 mg kg⁻¹ sulfadiazine for 40 days showed presence of the chemical in the roots at 333 and 26.5 mg kg⁻¹ dry weight, respectively, but not in the above-ground tissues (Michellini et al. 2012). Irrigation of soybean in greenhouse pots with water containing the pharmaceuticals carbamazepine, diphenhydramine, and fluoxetine each at 10 µg L⁻¹ for 60–110 days resulted in accumulation of carbamazepine but not diphenhydramine and fluoxetine in plant roots and leaves at 1.9–3.4 µg kg⁻¹ dry weight (Wu et al. 2010). As the concentrations of residual pharmaceuticals in agricultural soils receiving animal manures would be far lower compared with the levels tested in laboratory and greenhouse research, bioaccumulation of animal drugs in food crops, if there any, should be rather insignificant. So far it is not clear that bioaccumulation of veterinary chemicals in field crops poses health hazard to consumers of tainted plants.

2.4.5 Concentrations of Veterinary Pharmaceuticals in Manured Agricultural Soils

A few studies reported on low concentrations of veterinary pharmaceuticals detected in soils of cropland repeatedly receiving animal manure applications. The top 30-cm soils collected from a crop field immediately after cattle manure application at 96 ton ha⁻¹ demonstrated concentrations of oxytetracycline 6–7 µg kg⁻¹ and tylosin below the detection limit (De Liguoro et al. 2003). Hamscher et al. (2002, 2005) determined residual antibiotics in agricultural fields with sandy soils that were fertilized annually with livestock manure slurry at 30–50 m³ ha⁻¹ for many years in Northern Germany and detected 43–199 µg kg⁻¹ tetracycline, 3.7–7.3 µg kg⁻¹ chlortetracycline, but not any oxytetracycline, sulfamethazine, or tylosin in the top 30 cm soils. No antibiotics were present in deeper soils and only sulfamethazine was detected at 0.05–0.24 µg L⁻¹ in groundwater 140 cm below the surface. In Lansing (Michigan, USA) MI where concentrated livestock feeding operations exist, 0.03–0.26 µg kg⁻¹ amprolium and 0.004–0.50 µg kg⁻¹ monensin were detected in the top 10-cm sandy loam soils of the agricultural land (Song et al. 2010). Due to attenuation and degradation, veterinary pharmaceuticals generally have rather low concentrations (e.g., <10 µg kg⁻¹) and are mostly undetectable in soils of agricultural land receiving animal manure applications. So far contamination of food crops by plant absorption of the residual chemicals in manured agricultural soils has not been reported.

2.5 Ecological Impacts of Residual Veterinary Pharmaceuticals from Manures

Pharmaceutical antibiotics affect microorganisms even at low concentrations. The effects and effective doses vary with exposure time, microorganism species, and drug chemicals. The half maximal effective concentration (EC₅₀, the effective concentration that causes toxicity to 50 % of the test population) of chlortetracycline is 2.2 mg L⁻¹ for sewage sludge bacteria and that of tylosin is 54.7 mg L⁻¹ (Halling-Sørensen 2001). The EC₅₀ of monensin for soil respiration is 176 mg kg⁻¹ (Thiele-Bruhn 2003). Nevertheless, species of soil fauna such as earthworms, springtails, and enchytraeid worms are not influenced by antibiotics even at concentrations >100 mg kg⁻¹ (Bauger et al. 2000). The presence of chlortetracycline and oxytetracycline at 160 mg kg⁻¹ in loamy soils stimulated the nutrient uptake and promoted the growth of radish, wheat, and corn, but had little influence on bean growth (Batchelder 1982). In a loamy soil containing 109 mg kg⁻¹ sulfadimethoxine, the growth of barley was slightly inhibited (Migliore et al. 1996). Sulfadimethoxine at 300 mg L⁻¹ in a culture solution also restricted the growth of roots, hypocotyls, and leaves of pea, corn, and millet (Migliore et al. 1995). The antibiotics oxytetracycline and chlortetracycline at 5.3 and 11.3 mg kg⁻¹, respectively, in beef cattle feces

applied to a sandy loam at 18.8 dry ton ha⁻¹ enhanced soil respiration but did not influence the growth of corn seedlings (Patten et al. 1980). The fact is that land application of animal waste rarely results in residual antibiotics exceeding 0.2 mg kg⁻¹ in agricultural soils. These results suggest that at environmentally relevant concentrations, residual veterinary pharmaceuticals in manure-fertilized soils will not adversely affect soil microorganisms, fauna, and plants.

Residual veterinary pharmaceuticals may be transported to surface waters from manure-applied cropland. In surface ditches and drainage tile channels surrounding the cropland that repeatedly receives animal manure, an array of antibiotics have been detected in the water. Streams in agricultural watersheds also show the trace presence of veterinary pharmaceuticals. Fourteen antibiotics have been detected at concentrations by 44 ng L⁻¹ in seven tributaries of an agricultural watershed in Southern Ontario, Canada (Lissemore et al. 2006). A reconnaissance of 139 streams in the U.S. main continent detected 22 veterinary antibiotics in water at 0.014–0.10 µg L⁻¹ (Kolpin et al. 2002). Laboratory studies indicate that aquatic plants are the non-target organisms most sensitive to antibiotic chemicals. Of the 25 tested antibiotics of different chemical classes, lomefloxacin, sulfamethoxine, and chlor-tetracycline are most phytotoxic to duckweed (*Lemna gibba*), with EC₂₅ values of 38, 37, and 114 mg L⁻¹, respectively (Brain et al. 2004). At low concentrations (e.g., 0.3–3 mg L⁻¹) in water, antibiotics may enhance the growth of aquatic macrophytes (Solomon et al. 2010). In aquatic microcosm trials, effects of multiple antibiotics at concentrations below 0.22 µM were not observed on zooplankton, phytoplankton, and fishes (Richards et al. 2004; Wilson et al. 2004). The no-observed-effect concentrations of 15 tested veterinary pharmaceuticals in water to zebrafish (*Danio rerio*) embryos were around 0.02 mg L⁻¹ (Carlsson et al. 2013). This value of the parasiticide ivermectin to zooplankton was measured at 0.1 µg L⁻¹ (Boonstra et al. 2011). These no-observed-effect concentrations, however, were 40–100 times higher than maximum environmentally-relevant concentrations. Adverse exposure to veterinary pharmaceuticals in natural waters, if there is any, would be arid and semi-arid headwater streams adjacent to concentrated, confined livestock feeding operations (Brooks et al. 2006).

There is great concern on development and spread of antimicrobial resistance through heavy use and dispersion of veterinary pharmaceuticals in the environment. Common genes may mutate in the presence of antibiotics and resistance genes can transfer among diverse microorganisms. In animal intestinal guts live up to 10¹⁴ commensal bacteria of several hundred species (Andremont 2003). Antibiotic-resistant commensal bacteria may be selected every time when an antibiotic drug is administered. The bacteria are then excreted in animal feces and reach the environment through manure storage, handling, and disposal. In stored swine manure, 4–32 % of the bacteria, 71 % of the *Enterococcus fecalis* and 97 % of the *E. coli* were found resistant to at least one of the following antibiotics: tylosin, tetracycline, ampicillin, furatrizine, chloramphenicol, kanamycin, streptomycin, or sulfonamides (Haack and Andrews 2000; Cotta et al. 2003). These microorganisms survive the transition from manure storage lagoon into soil (Boes et al. 2005) and can be transported to surface water and groundwater via runoff and leaching processes (Unc and Goss 2003). Bacteria resistant to kanamycin and neomycin have been found in a coastal plain

stream in South Carolina (Left et al. 1993). A strain of superbug methicillin-resistant bacteria *Staphylococcus aureus* associated with antibiotic-fed animals was detected in the noses of livestock-handling workers in North Carolina and Iowa (Harrison et al. 2013; Rinsky et al. 2013). Transport of antibiotic-resistant bacteria and transfer of antibiotic-resistant genes in the environment were well reviewed by Chee-Sanford et al. (2009). Through conjugation (transfer of DNA between a donor and a recipient cell), transduction (bacteriophage-mediated transfer of DNA between bacterial cells), and transformation (transporting exogenous DNA into the cell cytoplasm and integrating the DNA into the recipient genome), antibiotic-resistant genes can be spread between different microbial genera and species (Chee-Sanford et al. 2009). Once antibiotic-resistant pathogens become predominant, the original drugs turn to be ineffective in treating the related infections. Disastrous losses of health and economy may occur if alternative treatment methods are not available. Banning the use of antibiotics in animal feed should root up the risk. To the bottom line, anaerobic digestion or thermophilic composting of animal waste can dramatically reduce the population of antibiotic-resistant microorganisms in manures (Sobsey et al. 2001; Cote et al. 2006).

2.6 Conclusion

The extensive use of veterinary pharmaceuticals, especially antibiotics as feed supplements in domestic animal production has resulted in significant discharge of the chemicals into the environment. In poultry, swine, and cattle manures, the residual contents of more than 50 major antibiotics were detected at 0.01–765 mg kg⁻¹ dry manure mass. On average, 50 % (10–90 %) of the administered veterinary pharmaceuticals were excreted as parent chemicals or bioactive metabolites in animal faeces and therefore, it was estimated that worldwide 3,000–27,000 tons of animal drugs entered into the natural ecosystem every year through manure disposal. In animal manures, pharmaceutical residues undergo microbial degradation and chemical transformation such as photolysis, hydrolysis, and decarboxylation. The half-lives of veterinary pharmaceuticals in animal manures ranged from less than 2 days to longer than 30 days. Composting or simply heaping for 60–90 days prior to manure land application is an effective way to eliminate the pharmaceutical residues. In soils, veterinary pharmaceuticals interact with soil minerals, organic matter, aqueous components, and organisms and are subject to sorption, photohydrolysis, oxidation, and biodegradation. Soil clay minerals and organic matter are both active agents for binding pharmaceuticals through a variety of mechanisms including van der Waals interaction, hydrophobic partitioning, electrostatic attraction, anion exchange, and cation bridging. However, the soil distribution coefficient (K_d) values of animal pharmaceuticals vary dramatically with the chemical species, from 0.3 to 6,300 L kg⁻¹. The persistence of veterinary pharmaceuticals in soils was influenced by a number of environmental factors such as soil type, organic matter content, pH, moisture content, and temperature. Most

pharmaceuticals are degradable in soils, demonstrating a half-life <30 days; whereas certain antibiotics such as roxithromycin, sarafloxacin, and virginiamycin were persistent and might remain unchanged in soils over months. In soils repeatedly receiving livestock manures for years, up to 200 $\mu\text{g kg}^{-1}$ of animal antibiotics were detected in the top 30-cm cultivation layer. Veterinary pharmaceuticals at such concentrations in soil would not impose discernible impacts on soil microorganisms, fauna, and plants, though plants and soil fauna could uptake and accumulate veterinary pharmaceuticals. So far contamination of food crops by residual pharmaceuticals in manured soils has not been reported. Even so, soil residual veterinary pharmaceuticals could diffuse from manured fields via surface runoff and deep percolation. Up to 290 ng L^{-1} of animal antibiotics were detected in drainage water from manure-fertilized cropland. In US and Canada, 22 animal antibiotics were detected in rivers and streams at up to 100 ng L^{-1} , though a concentration lower than the no-observed-effect concentrations of veterinary pharmaceuticals to aquatic organisms. The standing concern associated with heavy use of animal pharmaceuticals is development of antimicrobial resistance and spread antibiotic-resistant bacteria through manure disposal. To eliminate the risk, reducing and eventually banning the use of antibiotics in animal feed should be enacted.

2.7 Outlook on Practical Applications

Eliminating residual veterinary pharmaceuticals and antibiotic-resistant pathogens from livestock manure prior to land disposal of the waste is essential. Development of standard composting protocols and other effective methods for sterilizing animal manure should be a focus of future research. Composting is practical for on-farm operations and will also be able to eradicate animal-borne hormones. Prevention of pathogens from spreading from manure storage, handling, and composting facilities via runoff should be reinforced. Liquid from manure lagoons should be disinfected before environmental discharge. Since the long-term ecological impacts of veterinary pharmaceuticals at low concentrations in soil, water, and plants are largely unknown and are difficult to monitor, use of veterinary pharmaceuticals as feed additives should be gradually phased out. Research should advocate and assist in “sustainable, green animal-feed operations” by identifying alternative methods for enhancing animal health and growth.

References

- Accinelli C, Koskinen WC, Becker JM, Sadowsky MJ (2007) Environmental fate of two sulfonamide antimicrobial agents in soil. *J Agric Food Chem* 55:2677–2682
- Al-Ahmad A, Daschner FD, Kümmerer K (1999) Biodegradability of cefotiam, ciprofloxacin, meropenem, penicillin G, and sulfamethoxazole and inhibition of waste water bacteria. *Arch Environ Contam Toxicol* 37:158–163

- Allaire SE, Del Castillo J, Juneau V (2006) Sorption kinetics of chlortetracycline and tylosin on sandy loam and heavy clay soils. *J Environ Qual* 35:969–972
- Andremont A (2003) Commensal flora may play key role in spreading antibiotic resistance. *ASM News* 69:601–607
- Batchelder AR (1982) Chlorotetracycline and oxytetracycline effects on plant growth and development in soil systems. *J Environ Qual* 11:675–678
- Bauger AJ, Jensen J, Krogh PH (2000) Effects of the antibiotics oxytetracycline and tylosin on soil fauna. *Chemosphere* 40:751–757
- Beausse J (2004) Selected drugs in solid matrices: a review of environmental determination, occurrence and properties of principal substances. *Trends Anal Chem* 23:753–761
- Blackwell PA, Kay P, Boxall ABA (2007) The dissipation and transport of veterinary antibiotics in a sandy loam soil. *Chemosphere* 67:292–299
- Boes J, Alban L, Bagger J, Mongelmoose V, Baggsen DL, Olsen JE (2005) Survival of *Escherichia coli* and *Salmonella typhimurium* in slurry applied to clay soil on a Danish swine farm. *Prev Vet Med* 69:213–228
- Boonstra H, Reichman EP, van den Brink PJ (2011) Effects of the veterinary pharmaceutical ivermectin in indoor aquatic microcosms. *Arch Environ Contam Toxicol* 60:77–89
- Boxall BAB (2008) Fate of veterinary medicines applied to soil. In: Kümmerer K (ed) *Pharmaceuticals in the environment: sources, fate, effects and risks*. Springer, Berlin/Heidelberg, pp 103–119
- Brain RA, Johnson DJ, Richards SM, Sanderson H, Sibley PK, Solomon KR (2004) Effects of 25 pharmaceutical compounds to *Lemna gibba* using a 7-day static renewal test. *Environ Toxicol Chem* 23:371–382
- Brooks BW, Riley TM, Taylor RD (2006) Water quality of effluent dominated stream ecosystems: ecotoxicological, hydrological, and management considerations. *Hydrobiologia* 556:365–379
- Burkhardt M, Stamm C, Waul C, Singer H, Müller S (2005) Surface runoff and transport of sulfonamide antibiotics and tracers on manured grassland. *J Environ Qual* 34:1363–1371
- Campagnolo ER, Hohnson KR, Karpari A et al (2002) Antimicrobial residues in animal water and water resources proximal to large-scale swine and poultry feeding operations. *Sci Total Environ* 299:89–95
- Carballo EM, Barreiro CG, Scharf S, Gans O (2007) Environmental monitoring study of selected veterinary antibiotics in animal manure and soils in Austria. *Environ Pollut* 148:570–579
- Carlsson G, Patring J, Kreuger J, Norrgren L, Oskarsson A (2013) Toxicity of 15 veterinary pharmaceuticals in zebrafish (*Danio rerio*) embryos. *Aquat Toxicol* 126:30–41
- Chee-Sanford JC, Mackie RI, Koike S et al (2009) Fate and transport of antibiotic residues and antibiotic resistance genes following land application of manure waste. *J Environ Qual* 38:1086–1108
- Chefetz B, Muallem T, Ben-Ari J (2008) Sorption and mobility of pharmaceutical compounds in soil irrigated with reclaimed wastewater. *Chemosphere* 73:1335–1343
- Chen H, Gao B, Li H, Ma LQ (2011) Effects of pH and ionic strength on sulfamethoxazole and ciprofloxacin transport in saturated porous media. *J Contam Hydrol* 126:29–36
- Cote C, Masse DI, Quessy S (2006) Reduction of indicator and pathogenic microorganisms by psychrophilic anaerobic digestion in swine slurries. *Bioresour Technol* 97:686–691
- Cotta MA, Whitehead TR, Zeltwanger RL (2003) Isolation, characterization and comparison of bacteria from swine feces and manure storage pits. *Environ Microbiol* 5:737–745
- Davis JG, Truman CC, Kim SC, Ascough JC, Carlson K (2006) Antibiotic transport via runoff and soil loss. *J Environ Qual* 35:2250–2260
- De Liguoro M, Cibir V, Capolongo F et al (2003) Use of oxytetracycline and tylosin in intensive calf farming: evaluation of transfer to manure and soil. *Chemosphere* 52:203–212
- Dewey CE, Cox BD, Straw BE, Budh EJ, Hurd HS (1997) Association between off-label feed additives and farm size, veterinary consultant use, and animal age. *Prev Vet Med* 31:133–146
- Ding Y, Teppen BJ, Boyd SA, Li H (2013) Measurement of associations of pharmaceuticals with dissolved humic substances using solid phase extraction. *Chemosphere* 91:314–319

- Doi AM, Stoskopf MK (2000) The kinetics of oxytetracycline degradation in deionized water under varying temperature, pH, light, substrate, and organic matter. *J Aquat Anim Health* 12:246–253
- Dolliver H, Kumar K, Gupta S (2007) Sulfamethazine uptake by plants from manure-amended soil. *J Environ Qual* 36:1224–1230
- Dolliver H, Gupta S, Noll S (2008) Antibiotic degradation during manure composting. *J Environ Qual* 37:1245–1253
- Donoho AL (1984) Biochemical studies on the fate of monensin in animals and in the environment. *J Anim Sci* 58:1528–1539
- Europa (2005) Ban on antibiotics as growth promoters in animal feed enters into effect. Europa press release, December 22, 2005. http://europa.eu/rapid/press-release_IP-05-1687_en.htm. Accessed 10 Dec 2012
- FDA (2010) 2009 summary report on antimicrobials sold or distributed for use in food-producing animals. Food and Drug Administration, Rockville. www.fda.gov/downloads/ForIndustry/UserFees/AnimalDrugUserFeeActADUFA/UCM231851.pdf. Accessed 5 Mar 2013
- FDA (2012) The Green Book – FDA approved products. Food and Drug Administration, Rockville. <http://www.accessdata.fda.gov/scripts/animaldrugsatfda>
- Furtula V, Huang L, Chambers PA (2009) Determination of veterinary pharmaceuticals in poultry litter and soil by methanol extraction and liquid chromatography-tandem mass spectrometry. *J Environ Sci Health B* 44:717–723
- Furtula V, Farrell EG, Diarrassouba F et al (2010) Veterinary pharmaceuticals and antibiotic resistance of *Escherichia coli* isolates in poultry litter from commercial farms and controlled feeding trials. *Poult Sci* 89:180–189
- Gao J, Pedersen JA (2005) Adsorption of sulfonamide antimicrobial agents to clay minerals. *Environ Sci Technol* 39:9509–9516
- Garrido Frenich A, Plaza-Bolanos P, Aguilera-Luiz MM, Martinez-Vidal JL (2010) Veterinary drugs and growth-promoting agent analyses. Nova Science, Hauppauge
- Gartiser S, Urich E, Alexy R, Kümmerer K (2007) Ultimate biodegradation and elimination of antibiotics in inherent tests. *Chemosphere* 67:604–613
- Gaskins HR, Collier CT, Anderson DB (2002) Antibiotics as growth promotants: mode of action. *Anim Biotechnol* 13:29–42
- Gavalchin J, Katz SE (1994) The persistence of fecal-borne antibiotics in soil. *J AOAC Int* 77:481–485
- Gilbertson TJ, Hornish RE, Jaglan PS et al (1990) Environmental fate of ceftiofur sodium, a cephalosporin antibiotic. Role of animal excreta in its decomposition. *J Agric Food Chem* 38:890–894
- Gruber VF, Halley BA, Hwang SC, Ku CC (1990) Mobility of avermectin B1a in soil. *J Agric Food Chem* 38:886–890
- Gu C, Karthikeyan KG, Sibley SD, Pedersen JA (2007) Complexation of the antibiotic tetracycline with humic acid. *Chemosphere* 66:1494–1501
- Haack BJ, Andrews RE (2000) Isolation of Tn916-like conjugal elements from swine lot effluent. *Can J Microbiol* 46:542–549
- Haller MY, Müller SR, McArdell CS, Alder AC, Suter MJ (2002) Quantification of veterinary antibiotics (sulfonamides and trimethoprim) in animal manure by liquid chromatography–mass spectrometry. *J Chromatogr A* 952:111–120
- Halling-Sørensen B (2001) Inhibition of aerobic growth and nitrification of bacteria in sewage sludge by antibacterial agents. *Arch Environ Contam Toxicol* 40:451–460
- Halling-Sørensen B, Nors Nielsen S, Lanzky PF et al (1998) Occurrence, fate and effects of pharmaceutical substances in the environment – a review. *Chemosphere* 36:357–393
- Hanschler G, Sczesny S, Höper H, Nau H (2002) Determination of persistent tetracycline residues in soil fertilized with liquid manure by high-performance liquid chromatography with electrospray ionization tandem mass spectrometry. *Anal Chem* 74:1509–1518

- Hamscher G, Pawelzick HT, Höper H, Nau H (2005) Different behavior of tetracyclines and sulfonamides in sandy soils after repeated fertilization with liquid manure. *Environ Toxicol Chem* 24:861–868
- Harrison EM, Paterson GK, Holden MTG et al (2013) Whole genome sequencing identifies zoonotic transmission of MRSA isolates with the novel *mecA* homologue *mecC*. *EMBO Mol Med* 5:509–515
- Hayes JR, English LL, Carr LE, Wagner DD, Joseph SW (2004) Multiple-antibiotic resistance of *Enterococcus* spp. isolated from commercial poultry production environments. *Appl Environ Microbiol* 70:6005–6011
- Henderson KD, Coats JR (2010) Veterinary pharmaceuticals in the environment: an introduction. In: Henderson KD, Coats JR (eds) *Veterinary pharmaceuticals in the environment*, vol 1018, ACS symposium series. American Chemical Society, Washington, DC, pp 3–7
- Holt JP (2008) Growth performance and the development of antibiotic resistant bacteria in swine fed growth-promoting antimicrobials. PhD thesis, North Carolina State University, Raleigh
- Hu D, Coats JR (2007) Aerobic degradation and photolysis of tylosin in water and soil. *Environ Toxicol Chem* 26:884–889
- Huang CH, Renew JE, Smeby KL et al (2001) Assessment of potential antibiotic contaminants in water and preliminary occurrence analysis. In: *Proceedings of the 2nd international conference on pharmaceuticals and endocrine disrupting chemicals in water*. Groundwater Association, Westerville, pp 46–57
- Jiao S, Zheng S, Yin D, Wang L, Chen L (2008) Aqueous photolysis of tetracycline and toxicity of photolytic products to luminescent bacteria. *Chemosphere* 73:377–382
- Jones AD, Bruland GL, Agrawal SG, Vasudevan D (2005) Factors influencing the sorption of oxytetracycline to soils. *Environ Toxicol Chem* 24:761–770
- Karci A, Balcioglu IA (2009) Investigation of the tetracycline, sulfonamide, and fluoroquinolone antimicrobial compounds in animal manure and agricultural soils in Turkey. *Sci Total Environ* 407:4652–4664
- Kim SC, Davis JG, Truman CC, Ascough Ii JC, Carlson K (2010) Simulated rainfall study for transport of veterinary antibiotics – mass balance analysis. *J Hazard Mater* 175:836–843
- Kishi H, Kogure N, Hashimoto Y (1990) Contribution of soil constituents in adsorption coefficient of aromatic compounds, halogenated alicyclic and aromatic compounds to soil. *Chemosphere* 21:867–876
- Kolpin DW, Furlong ET, Meyer MT et al (2002) Pharmaceuticals, hormones and other organic wastewater contaminants in US streams, 1999–2000: a national reconnaissance. *Environ Sci Technol* 36:1202–1211
- Kreuzig R, Holtge S, Brunotte J et al (2005) Test-plot studies on runoff of sulfonamides from manured soils after sprinkler irrigation. *Environ Toxicol Chem* 24:777–781
- Kulshrestha P, Giese RF, Aga DS (2004) Investigating the molecular interactions of oxytetracycline in clay and organic matter: insights on factors affecting its mobility in soil. *Environ Sci Technol* 38:4097–4105
- Kumar K, Thompson A, Singh AK, Chander Y, Gupta SC (2004) Enzyme-linked immunosorbent assay for ultratrace determination of antibiotics in aqueous samples. *J Environ Qual* 33:250–256
- Kumar K, Gupta SC, Baidoo SK, Chander Y, Rosen CJ (2005a) Antibiotic uptake by plants from soil fertilized with animal manure. *J Environ Qual* 34:2082–2085
- Kumar K, Gupta SC, Chander Y, Singh AK (2005b) Antibiotic use in agriculture and its impact on the terrestrial environment. *Adv Agron* 87:1–54
- Left LG, Dana JR, McArthur JV, Shimkets LJ (1993) Detection of Tn5-like sequences in Kanamycin-resistant stream bacteria and environmental DNA. *Appl Environ Microbiol* 59:417–421
- Lertpaitoonpan W, Ong SK, Moorman TB (2009) Effect of organic carbon and pH on soil sorption of sulfamethazine. *Chemosphere* 76:558–564

- Li XL, Zheng W, Machesky ML, Yates SR, Katterhenry M (2011) Degradation kinetics and mechanism of antibiotic ceftiofur in recycled water derived from a beef farm. *J Agric Food Chem* 59:10176–10181
- Li Y, Zhang X, Li W, Lu X, Liu B, Wang J (2013) The residues and environmental risks of multiple veterinary antibiotics in animal faeces. *Environ Monit Assess* 185:2211–2220
- Lin K, Gan J (2011) Sorption and degradation of wastewater-associated non-steroidal anti-inflammatory drugs and antibiotics in soils. *Chemosphere* 83:240–246
- Lissemore L, Hao C, Yang P et al (2006) An exposure assessment for selected pharmaceuticals within a watershed in southern Ontario. *Chemosphere* 64:717–729
- MacKay AA, Canterbury B (2005) Oxytetracycline sorption to organic matter by metal-bridging. *J Environ Qual* 34:1964–1971
- Marengo JR, Kok RA, O'Brien K et al (1997) Aerobic biodegradation of (14C)-Sarafloxacin hydrochloride in soil. *Environ Toxicol Chem* 16:462–471
- McEwen SA, Fedorka-Cray PJ (2002) Antimicrobial use and resistance in animals. *Clin Infect Dis* 34:S93–S106
- Michelini L, Reichel R, Werner W et al (2012) Sulfadiazine uptake and effects on *Salix fragilis L.* and *Zea mays L.* plants. *Water Air Soil Pollut* 223:5243–5257
- Migliore L, Brambilla G, Cozzolina S, Gaudio L (1995) Effect on plants of sulphadimethoxine used in intensive farming (*Panicum miliaceum*, *Pisum sativum* and *Zea mays*). *Agric Ecosyst Environ* 52:103–110
- Migliore L, Brambilla G, Casoria P et al (1996) Effect of sulphadimethoxine contamination on barley (*Hordeum distichum L.*, Poaceae, Liliopsida). *Agric Ecosyst Environ* 60:121–128
- Nowara A, Burhenne J, Spiteller M (1997) Binding of fluoroquinolone carboxylic acid derivatives to clay minerals. *J Agric Food Chem* 45:1459–1463
- OTA (1979) Drugs in livestock feed. NTIS order #PB-298450. Office of Technology Assessment, Congress of the United States, Washington, DC
- Paesen J, Cypers W, Busson R et al (1995) Isolation of decomposition products of tylosin using liquid chromatography. *J Chromatogr A* 699:99–106
- Pan X, Qiang Z, Ben W, Chen M (2011) Residual veterinary antibiotics in swine manure from concentrated animal feeding operations in Shandong Province, China. *Chemosphere* 84:695–700
- Patten DK, Wolf DC, Kunkle WE, Douglass LW (1980) Effects of antibiotics in beef cattle feces on nitrogen and carbon mineralization in soil and plant growth and composition. *J Environ Qual* 9:167–172
- Pils JRV, Laird DA (2007) Sorption of tetracycline and chlortetracycline on K- and Ca-saturated soil clays, humic substances, and clay–humic complexes. *Environ Sci Technol* 41:1928–1933
- Rabølle M, Spliid NH (2000) Sorption and mobility of metronidazole, olaquinox, oxytetracycline, and tylosin in soil. *Chemosphere* 40:715–722
- Richards SM, Wilson CJ, Johnson DJ et al (2004) Effects of pharmaceutical mixtures in aquatic microcosms. *Environ Toxicol Chem* 23:1035–1042
- Rinsky JL, Naimpalli M, Wing S et al (2013) Livestock-associated methicillin and multidrug resistant *Staphylococcus aureus* is present among industrial, not antibiotic-free livestock operation workers in North Carolina. *PLoS One* 8(7):e67641. doi:10.1371/journal.pone.0067641
- Sarmah AK, Meyer MT, Boxall ABA (2006) A global perspective on the use, sales, exposure pathways, occurrence, fate and effects of veterinary antibiotics (VAs) in the environment. *Chemosphere* 65:725–759
- Sassman SA, Lee LS (2005) Sorption of three tetracyclines by several soils: assessing the role of pH and cation exchange. *Environ Sci Technol* 39:7452–7459
- Sassman SA, Lee LS (2007) Sorption and degradation in soils of veterinary ionophore antibiotics: monensin and lasalocid. *Environ Toxicol Chem* 26:1614–1621

- Schlüsener MP, Bester K (2006) Persistence of antibiotics such as macrolides, tiamulin and salinomycin in soil. *Environ Pollut* 143:565–571
- Sengeløv G, Halling-Sørensen AB, Baloda SB et al (2003) Bacterial antibiotic resistance levels in Danish farmland as a result of treatment with pig manure slurry. *Environ Int* 28:587–595
- Sibley SD, Pedersen JA (2008) Interaction of the macrolide antimicrobial clarithromycin with dissolved humic acid. *Environ Sci Technol* 42:422–428
- Sithole BB, Guy RD (1987) Models for tetracycline in aquatic environments: I. Interaction with Bentonite clay systems. *Water Air Soil Pollut* 32:303–314
- Smith SC, Ainsworth CC, Traina SJ, Hicks RJ (1992) Effect of sorption on the biodegradation of quinoline. *Soil Sci Soc Am J* 56:737–746
- Sobsey MD, Khatib LA, Hill MR et al (2001) Pathogens in animal wastes and the impacts of waste management practices on their survival, transport and fate. White Paper Summaries. www.cals.ncsu.edu/waste_mgt/natcenter/whitepaperstimmaries/pathogens.pdf. Accessed 29 Dec 2012
- Solomon KR, Hillis DG, Lissemore L, Sibley PK (2010) Risks of agricultural pharmaceuticals in surface water systems and soils. In: Henderson K et al (ed) *Veterinary pharmaceuticals in the environment*, ACS symposium series. American Chemical Society, Washington, DC, pp 191–204
- Song W, Ding Y, Chiou CT, Li H (2010) Selected veterinary pharmaceuticals in agricultural water and soil from land application of animal manure. *J Environ Qual* 39:1211–1217
- Swift RS (1996) Organic matter characterization. In: Sparks DL (ed) *Methods of soil analysis*, Part 3. Chemical methods. Soil Science Society of America, Madison, pp 1011–1069
- Thiele-Bruhn S (2003) Pharmaceutical antibiotic compounds in soils: a review. *J Plant Nutr Soil Sci* 166:145–167
- Thiele-Bruhn S, Aust MO (2004) Effects of pig slurry on the sorption of sulfonamide antibiotics in soil. *Arch Environ Contam Toxicol* 47:31–39
- Thiele-Bruhn S, Seibicke T, Schulten HR, Leinweber P (2004) Sorption of sulfonamide pharmaceutical antibiotics on whole soils and particle-size fractions. *J Environ Qual* 33:1331–1342
- Tolls J (2001) Sorption of veterinary pharmaceuticals in soils: a review. *Environ Sci Technol* 35:3397–3406
- Unc A, Goss MJ (2003) Movement of fecal bacteria through the vadose zone. *Water Air Soil Pollut* 149:327–337
- von Nussbaum F, Brands M, Hinzen B et al (2006) Medicinal chemistry of antibacterial natural products – exodus or revival? *Angew Chem Int Ed* 45:5072–5129
- Wang Q, Guo M, Yates SR (2006) Degradation kinetics of manure-derived sulfadimethoxine in amended soil. *J Agric Food Chem* 54:157–163
- Wang YJ, Jia DA, Sun RJ, Zhu HW, Zhou DM (2008) Adsorption and cosorption of tetracycline and copper(II) on montmorillonite as affected by solution pH. *Environ Sci Technol* 42:3254–3259
- Wang C, Teppen BJ, Boyd SA, Li H (2012) Sorption of lincomycin at low concentrations from water by soils. *Soil Sci Soc Am J* 76:1222–1228
- Warman PR, Thomas RL (1981) Chlortetracycline in soil amended with poultry manure. *Can J Soil Sci* 61:161–163
- Weerasinghe CA, Towner D (1997) Aerobic biodegradation of virginiamycin in soil. *Environ Toxicol Chem* 16:1873–1876
- Wetzstein HG, Stadler M, Tichy HV et al (1999) Degradation of ciprofloxacin by basidiomycetes and identification of metabolites generated by the brown rot fungus *Gloeophyllum striatum*. *Appl Environ Microbiol* 65:1556–1563
- Wilson CJ, Brain RA, Sanderson H et al (2004) Structural and functional responses of plankton to a mixture of four tetracyclines in aquatic microcosms. *Environ Sci Technol* 38:6430–6439
- Witte W (2000) Selective pressure by antibiotic use in livestock. *Int J Antimicrob Agents* 16:S19–S24

- Wu CX, Spongberg AL, Witter JD et al (2010) Uptake of pharmaceutical and personal care products by soybean plants from soils applied with biosolids and irrigated with contaminated water. *Environ Sci Technol* 44:6157–6161
- Yeager RL, Halley BA (1990) Sorption/desorption of [¹⁴C]efrotomycin with soils. *J Agric Food Chem* 38:883–886
- Zhao L, Dong YH, Wang H (2010) Residues of veterinary antibiotics in manures from feedlot livestock in eight provinces of China. *Sci Total Environ* 408:1069–1075
- Zitnick KK, Shappell NW, Hakk H et al (2011) Effects of liquid swine manure on dissipation of 17beta-estradiol in soil. *J Hazard Mater* 186:1111–1117
- Zou Y, Zheng W (2013) Modelling manure colloid-facilitated transport of the weakly hydrophobic antibiotic florfenicol in saturated soil columns. *Environ Sci Technol* 47:5185–5192



<http://www.springer.com/978-94-017-8806-9>

Applied Manure and Nutrient Chemistry for Sustainable
Agriculture and Environment

He, Z.; Zhang, H. (Eds.)

2014, X, 379 p. 107 illus., 38 illus. in color., Hardcover

ISBN: 978-94-017-8806-9