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Abstract

A total of 59 papers published in 2015 were reviewed ranging from detailed descriptions of analytical methods, to fate and occurrence studies, to ecological effects and sampling techniques for a wide variety of emerging contaminants likely to occur in agricultural environments. New methods and studies on veterinary pharmaceuticals, steroids, antibiotic resistance genes in agricultural environments continue to expand our knowledge base on the occurrence and potential impacts of these compounds. This review is divided into the following sections: Introduction, Analytical Methods, Steroid Hormones, Pharmaceutical Contaminants, Transformation Products, and "Antibiotic Resistance, Drugs, Bugs and Genes".

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Keywords

pharmaceuticals; steroid hormones; anthelmintics; analytical methods; water and wastewater; agricultural environments

INTRODUCTION

Water resources in agricultural environments are impacted by a wide variety of contaminants including nutrients, sediments, and pesticides. These groups of contaminants typically occur at easily measured concentrations in surface run–off in agricultural watersheds. Nutrients, especially nitrogen, and pesticides have also been shown to impact ground water quality in areas susceptible to contamination. The impacts of newer contaminant classes such as pharmaceuticals, steroids, antibiotics and antibiotic–resistance genes of bacteria are less well-known. These “emerging” contaminants clearly have potential to enter the environment and cause known or suspected adverse ecological or human health effects. Release of these contaminants to the environment has very likely occurred for quite some time, but methods for their detection at environmentally–relevant concentrations have only recently become available.

Evaluating the environmental fate and effects of emerging contaminants includes compounds such as surfactants, antibiotics and other pharmaceuticals, steroid hormones and other endocrine–disrupting compounds (EDCs), fire retardants, sunscreens, disinfection byproducts, new pesticides and pesticide metabolites, and naturally–occurring algal toxins. Detection of these contaminants in environmental matrices (water, wastewater, soils and sediments) is particularly challenging because of the low detection limits required, the complex nature of the samples, and difficulty in separating these compounds from interferences. New extraction and clean–up techniques, coupled with improvements in instrumental technologies provide the needed sensitivity and specificity for accurate measurement.

The objective of this section is to review the literature published in 2015 evaluating the detection, fate, and occurrence of emerging contaminants, with a particular focus on those contaminants likely to be found in agricultural systems. Relevant contaminants are EDCs (particularly hormones and anabolic steroids), antibiotics and other pharmaceuticals associated with wastewater, as well as antibiotic resistance genes and bacteria. Studies on pesticides and flame retardants are not reviewed unless they were evaluated in the same study.

ANALYTICAL METHODS

New developments in analytical methods permit more rapid and sensitive and simplified analysis of emerging contaminants in agricultural environments. For example, Backe (2015) presents an ultrasensitive method for the detection of estrogens (17β-estradiol, estrone, estriol, 17α-ethinylestradiol, and equilin) in surface water which utilized liquid-liquid extraction followed by dansyl chloride derivatization and large volume injection (100 μL) coupled to liquid chromatography tandem mass spectrometry (LC-MS/MS). Detection limits

ranging from 0.030 ng/L for estriol to 0.13 ng/L for equilin with accuracies ranging from 93±5.8% to 105±4.5%. Tandem mass spectrometry (MS/MS) detection and positive electrospray ionization (ESI) was optimized for each analyte. The estrogens 17β-estradiol, estrone, estriol, and 17α-ethinylestradiol were quantified by the use of isotope dilution. Results from method validation and application of the method for samples containing Mississippi River wastewater treatment plant effluent are presented and show decreasing concentrations with distance downstream. Estrone was detected in the effluent samples up to 0.63 ng/L.

A simplified extraction and cleanup method was described by Camilleri and Vulliet (2015) for use in the analysis of steroid hormones in river sediments with LC-MS/MS. Electrospray ionization in both positive (testosterone, progesterone, megestrol acetate, and tamoxifen) and negative (estrone and 17β-estradiol) modes were used for detection. Optimization of a "QuEChERS" extraction protocol reduced interferences which could cause matrix effects during the analysis. Detection limits between 0.03 and 0.2 ng/g were obtained with recoveries greater than 74%. Results from analyses of Bourbre River (France) water revealed the presence of estrone and tamoxifen at concentrations up to ~40 ng/g and ~0.6 ng/g, respectively.

Melo et al. (2015) presented a method using *in-situ* derivation for gas chromatography mass spectrometry (GC/MS) analysis of endocrine disruptors in water samples. 17β-estradiol, estrone, 17α-ethinylestradiol, and bisphenol A (BPA) were detected as their acetate derivatives after dispersive liquid–liquid microextraction (DLLME) of the water sample. Reported detection limits of 0.003–0.005 μg/L were obtained with recoveries of 86.4 to 118.2%. Optimization of the conditions, such as concentration of salting out agent, extraction solvent, and buffer amount, for the extraction and derivatization of the analytes are discussed.

González et al. (2015) used a novel in-syringe magnetic stirring-assisted dispersive liquid–liquid microextraction (in-syringe-MSA-DLLME) with trimethylsilyl derivatization to analyze estrogens (estrone, 17β-estradiol, estriol, and 17α-ethinylestradiol) by GC/MS. Results from the optimization of extraction and derivatization parameters are presented. Detection limits between 11 and 82 ng/L were obtained for a 4.55 mL sample, comparable or lower to other DLLME and solid phase extraction (SPE) methods in the literature when the mass detection limit is calculated. Application of the method on fortified wastewater from sewage treatment plants yielded recoveries between 85 and 116%.

Cross-reactivity of two commercially available molecularly imprinted SPE polymers (AFFINIMIP®SPE *Estrogens* and AFFINIMIP®SPE *Zearalenone*) were compared by González-Sálamo et al. (2015) for extraction of steroid hormones in water. Extraction of 12 estrogenic compounds (comprised of estrogens and zearalenols) from various water sources found that cross-reactivity was high for both polymers for purified water but for mineral water and wastewater, the *Zearalenone* polymer was able to extract a larger quantity of the non-target steroid than the Estrogen polymer. Analyte concentrations were obtained by LC-MS/MS in negative electrospray mode. Validation of results in the extraction of wastewater

produced detection limits between 0.01 and 0.32 μg/L with relative standard deviation (RSD) below 16%.

Jonker et al. (2015) correlated LC-MS/MS concentrations between a screening method using human cell (BG1.Luc) gene reporter assays in identification of estrogenic and anti-estrogenic compounds in water. Tandem MS/MS analyses were obtained in parallel with high resolution online fraction collection which enabled direct compariсon of the mass spectrometric data with the bioassay results. The bioassay testing enables detection of estrogenic compounds in situations where difficult sample matrices, non-targeted MS screens, or low concentrations might not reveal the presence of endocrine active compounds. Detection limits of 80 nM, 320 pM and 3.2 nM were obtained for bisphenol A, estradiol, and estriol, respectively.

Berge and Vulliet (2015) developed a method to measure pharmaceuticals and steroid hormones in earthworms using a QuEChERS extraction kit with LC-MS/MS detection. Recovery and sensitivity for 14 veterinary antibiotics, 11 steroids, and 6 human pharmaceutical contaminants, were evaluated in the method. Mass spectra was collected in both positive and negative ESI modes. Detection limits of less than 14 ng/g were obtained for all compounds with recoveries between 44% and 98%. Results from exposed earthworm samples showed maximum concentrations for each group of analytes to be 195 ng/g for bisphenol A, 73.5 ng/g for florfenicol, and 43.1 ng/g for estrone. The authors indicate that earthworms may a useful tracer of human impact on soil ecosystems.

Many chiral forms of pharmaceuticals occur in agricultural environments and because each form may have unique biological properties, there is continuing interest in methods for measuring specific enantiomers. An enantiomer selective method for the analysis of chiral pharmaceuticals in water and wastewater was described by Camacho-Munoz and Kasprzyk-Hordern (2015). Using a chiral column and detection via positive electrospray MS/MS, chromatographic separation of enantiomers was achieved for ibuprofen, chloramphenicol, naproxen, ifosfamide, fexofenadine, tetramisole, and their metabolites was possible while partial separation was obtained for praziquantel and ketoprofen. Recoveries were found to be greater than 70% for most compounds with nanogram per liter detection limits. The method was applied to samples of surface water and wastewater effluent in England. Among the reported results was that R-(−)-ibuprofen and the more therapeutically active isomer, S-(+)-ibuprofen, were found at concentrations of 0.24±0.04 μg/L and 0.46±0.06 μg/L, respectively.

Chuang et al. (2015) described a cleanup method using QuEChERS kits for the extraction of 11 target pharmaceuticals (acetaminophen, caffeine, carbadox, carbamazepine, lincomycin, monensin (Na), oxytetracycline, sulfadiazine, sulfamethoxazole, trimethoprim and tylosin) in vegetables with detection by Turbo IonSpray MS/MS in positive mode. Recoveries of the target compounds ranged from 70.1& to 118.6% with detection limits at the low nanogram per gram level. A comparison of the QuEChRS extraction method to a method using accelerated solvent extraction (ASE) are presented for celery and lettuce matrices. The results indicated that the QuEChERS method performed better or equivalent to the ASE method with lower solvent volumes and reduced sample preparation costs.

A simple method to quantify 12 aminoglycosides in wastewater was proposed by Mokh et al. (2015) (2015) using solid phase extraction (SPE) and positive electrospray MS/MS. The authors compared two SPE cartridge phases, a modified reversed-phase C18 phase with pentafluoropropionic acid (PFPA) as an ion pairing agent, and a polymeric mixed mode cation exchange SPE. The C18 cartridge with PFPA gave better recoveries than the cation exchange, especially for streptomycin and dihydrostreptomycin. The validated method was reported to have detection limits between 5 ng/L and 50 ng/L with recoveries between 65% and 115%. The method was applied to samples from two wastewater treatment plants and one veterinary hospital effluent, and gentamycin was detected at 30 ng/L in one sample.

Xue et al. (2015) optimized a method using UPLC/MS/MS for the analysis of 35 antibiotics, including lincomycin, chloramphenicol, and other analytes from the compound classes of sulfonamides, quinolones, macrolides, and tetracyclines, from ground water, surface water, and wastewater. Extraction using Oasis HLB™ SPE cartridges were optimized and analytes were detected in positive electrospray ionization mode using 0.1% formic acid in the mobile phase. Detection limits between 0.29 ng/L and 4.03 ng/L were obtained with recoveries between 68.9% and 92.7%.

SPE was combined with LC-MS/MS by Yi et al. (2015) for sensitive measurement of antibiotics in surface waters and soils. Adjustment of sample pH influenced the recovery efficiency of both acidic and basic antibiotics. Optimization of extraction conditions resulted in detection limits with positive ion electrospray between 0.06 ng/L and 2.3 ng/L from surface waters and between 0.01 ng/g and 18.2 ng/g (dry wt.) for soils. Application of the method to urban samples found sulfonamides, macrolides, and lincomycin were the most frequently detected antibiotics with the highest concentrations of 82.5 ng/L sulfamethazine in surface waters and of 6.6 ng/g (dry wt.) erythromycin in soils.

STEROID HORMONES

The occurrence, fate, and ecological effects of steroid hormones in agricultural environments continues to be of interest. Zhang et al. (2015) detected estrone, 17α-estradiol, 17β-estradiol, estriol, testosterone, androstenedione and progesterone in the soil, the drainage ditch, and the groundwater of an intensively cultivated area with several years of manure application at a rate of 1.3 – 17.1 $kg \cdot m^{-2}$. The detection frequency of these seven steroids in the soil samples ranged from 3.13% (estriol) to 100% (progesterone and androstenedione). Progesterone, androstenedione and estrone occurred in the soil at the highest levels with maximum concentrations of 109.7, 9.83 and 13.3 $\mu g \cdot kg^{-1}$, respectively. However, their concentrations in the groundwater samples were lower than the other steroids or below the detection limit (estrone). The detection frequencies of estriol, testosterone, 17α-estradiol, and 17β-estradiol in the groundwater were 69.2%, 38.5%, 23.1% and 23.1%, respectively, with the concentrations up to 2.38 ng/L. All seven steroids were found in the drainage ditch sediment with average concentrations of 0.05 – 2.94 μg/kg. Six of the steroid hormones were detected in drainage ditch water, with concentrations ranging from below the detection limit to 14 ng/L.

Hansen et al. (2015) evaluated the potential of manure separation systems to reduce the release of steroid hormones to the environment from animal manure. Raw manure and the liquid and solid fractions separated from raw manure were collected from ten swine farms and their manure separation systems. All the samples were analyzed for nine steroids including pregnenolone, progesterone, dehydroepiandrosterone, androstenedione, testosterone, dehydrotestosterone, estrone, 17α-estradiol and 17β-estradiol using isotope dilution gas chromatography tandem mass spectrometry. Their results suggested that separation of livestock manure into a liquid and a solid fractions and only applying the liquid to the filed could reduce the steroid hormone loading by a factor of 2 without trading off the nitrogen application rate.

Sorption and desorption

Ma et al. (2015) suggested that clay content, soil organic matter, temperature, ionic strength, water/soil ratio, and soil depth affected the sorption and desorption of testosterone in soil. The Freundlich sorption coefficients K_f of the four agricultural soils and the five clay minerals evaluated were 8.53–74.46 and 35.28–1,243 (μg/g)/(μg/mL)^n, respectively. The soil sorption capacity ranged from 25.25 to 440.61 μg/g and the clay ranged from 168.46 to 499.84 μg/g. Increasing temperature decreased the sorption capacity of soils. 14%–100% of adsorbed testosterone can desorb after three desorption cycles, and a positive correlation has been be observed between desorption percentage of testosterone and three factors including the initial testosterone concentration, the soil depth as well as the water/soil ratio.

Sangster et al. (2015) evaluated the sorption capacity of different particles size fractions separated from a silt loam and a sandy sediments as well as the distribution of 17β-estradiol, estrone, progesterone and testosterone among different size particles within the whole sediments. Fine textured particles (clay and colloid fractions) of both sediment exhibited larger sorption capacities for the four steroids compared to the sand and silt fractions. The authors suggested that the sorption capacities were affected more by organic carbon content than particle size. Preferential sorption of the four steroids to the fine particles within whole sediments were observed, supported by the larger linear sorption coefficients of fine particles relative to those of coarse particles.

Steroid Transformation

Blackwell et al. (2015) investigated the biotransformation of trenbolone acetate metabolites and estrogen conjugates in the feces and urine of beef cattle just implanted with a formula of 200 mg trenbolone acetate and 40 mg 17β-estradiol. The results show that glucuronide and sulfate conjugates of 17α-trenbolone and 17α-estradiol were predominant in fresh urine but were not present in feces. Steroid conjugates in urine were transformed to free steroids rapidly with a half-life of 0.6–1.0 day. The half-lives of 17α-trenbolone and 17α-estradiol were 5.1–9.5 days and 8.6–53 days, respectively, longer than those reported in aerobic soils. 10% of initial 17α-trenbolone was transformed to secondary metabolites (trendione and 17β-trenbolone). Estrone and 17β-estradiol were formed from the biotransformation of 17α-estradiol, and concentrations of estrone were higher than the initial 17α-estradiol concentration. This study suggests that steroid hormones are more persistent in manure than

in aerobic soil and thus the runoff or airborne particulate matter directly from feedyard pens are of concerns.

Cole et al. (2015) also evaluated the biotransformation rates of 17β-trenbolone, 17α-trenbolone, and trendione in inoculated microcosms and the impact of incubation temperature. In addition to interconversion between these three androgens, other transformation products and potential transformation pathways were also proposed based on the analysis by high-resolution liquid chromatography-tandem mass spectrometry. Half-lives (20°C) estimated from the models of best fit were 0.9 d for 7β-trenbolone, 1.3 d for trendione, and 2.2 d for 17α-trenbolone. Transformation rates observed at 5°C were smaller than those at 20°C. 1,2 dehydro-products and hydroxyl-1,2 dehydro-products were proposed as the major products transformed from 17β-trenbolone, 17α-trenbolone, and trendione. The preservation of the steroidal structure of these dehydro-products indicated their bioactivity.

PHARMACUETICAL CONTAMINANTS

Contaminants of emerging concern (CECs) including veterinary medicines were studied in a mixed use watershed in Minnesota, USA Fairbairn et al. (2015). This study found a seasonal variation in aqueous concentrations, though associated sediment concentrations were relatively consistent. In addition, spatial distribution was related to land use and while hydrophobic partitioning did not govern sediment-water distribution, increasing hydrophobicity and persistence of a compound increased the predictability of distribution coefficients. Topal (2015) evaluated the uptake of the antibiotic tetracycline and three TPs in *Phragmites australis*, the common reed. The study revealed that TPs were detected at higher concentrations in both water and sediment with corresponding higher concentrations in the plants. Highest concentrations of the parent compound and TPs were detected in roots followed by shoots and leaves showing inefficient translocation of the contaminants by the plant.

The occurrence of veterinary antibiotics, such as monensin, lincomycin, and sulfamethazine, has been reported in surface water, groundwater, and soil across the world. Jaimes-Correa et al. (2015) evaluated the temporal variations occurrence of 12 veterinary antibiotics, including lincomycin, sulfamethazine and monensin, and a beta agonist in an intensively agricultural watershed, Shell Creek, NE. Monensin (94.5%), sulfamethazine (94.5%) and lincomycin (85.5%) were among the most commonly detected veterinary antibiotics. The antibiotics measured at the highest time-weighted average concentrations were lincomycin (68 ngL-1) and monensin (49 ngL-1), and both compounds were detected at increased concentrations in summer months driven by rainfall-runoff events. Sulfamethazine had a maximum concentration of 13 ngL-1 detected in October (Jaimes-Correa et al 2015).

Li et al (2015) investigated the occurrence of 15 antibiotics, including sulfamethazine, in soil and manure samples from 11 large-scale greenhouse vegetable production bases in Beijing, China. The occurrence of sulfamethazine ranged between 23.2% (greenhouse soils) and 58.8% (manure), while the mean ranged between 0.05 ng/g (open field soil) and 7.5 ng/g (manure). The highest concentration of sulfamethazine, ng/g, was observed in the manure (Li et al 2015).

Ma et al. (2015) investigated the occurrence of 20 antibiotics during the groundwater recharge process across China. Fifteen locations employing reclaimed water located in different humid, semi-humid and semi-arid regions were identified, and samples of both reclaimed and ground water were analyzed. Sulfamethazine occurred in 46.7% of the groundwater samples compared to 53.3% of reclaimed water. The highest concentrations ranged between 49 ng/g in groundwater samples compared to 469 ng/L in reclaimed water.

Ou et al. (2015) investigated the occurrence of 9 sulfonamide antibiotics, including sulfamethazine, in the downstream and estuarine areas of Jiulong River, China, during the rainy and dry seasons. Sulfamethazine exhibited the highest concentration and detection frequency, with a concentration of 0–53.41 ng/L and 4.84–138.66 ng/L, with a detection rate of 16.67% and 100% in August 2011 and May 2012, respectively. In a survey of 1153 organic micropollutants evaluated in the aquatic environment of Vietnam, Chau et al. (2015) detected 13 antibiotics, including the veterinary antibiotic lincomycin. The maximum concentration of lincomycin in surface water was 2.66 ng/L.

Bailey et al. (2015) investigated overland transport and potential impact of 15 veterinary antibiotics, including sulfamethazine, on German surface water quality. Three sampling schemes 1) seasonal, 2) post-flood and 3) high usage sampling were simulated. Sulfamethazine was only detected under post-flood sampling in one of the five sampling sites at concentrations below 20 ng/L.

Anthelmintic Drugs

Anthelmintic drugs, used for the treatment of infection caused by helminths (parasitic worms), can have either a broad or narrow spectrum of anti-parasitic activity and are widely used in livestock production. Broad spectrum anthelmintics are used to treat lungworm and gastrointestinal nematode infections, while the narrow spectrum products are predominantly used to treat liver and rumen fluke infections (Cooper et al. (2015)). The benzimidazoles (albendazole, fenbendazole, medendazole, oxfendazole and ricobendazole), levamisole, the avermectins (abamectin, doramecin, eprinomectin and ivermectin), moxidectin, and the amino-acetonitrile derivatives (ACD) are examples of anthelmintics with a broad spectrum, while clorsulon, closantel, nitroxynil, oxyclozanide and triclabendazole have a narrow spectrum of anti-parasitic activity. Research in these emerging contaminants continues to growth.

Brown et al. (2015) evaluated the downstream fate of 25 pharmaceuticals, including one anthelmintic compounds (thiabendazole), in wastewater-influenced surface waters. Samples were collected in the effluent before discharge, in the receiving stream within the effluent mixing zone, 500 m and 1500 m downstream from the effluent discharge. At the Lincoln location, thiabendazole ranged between 1.9 ± 0.6 ng/L (mixing zone) to 0.6 ± 0.1 ngL^{-1} approximately 1500 m downstream from the effluent discharge. At the Hastings location, thiabendazole ranged between 1.8 ± 0.3 ng/L in effluent before discharge to 0.8 ± 0.1 ng/L approximately 1500 m downstream from the effluent discharge. First-order decay rates for thiabendazole were estimated at both sites, corresponding to dissipation half-lives ranging between of 1.9 and 22 h depending on characteristics of the river.

Moreno-González et al. (2015) investigated the occurrence and seasonal distribution of 50 pharmaceuticals in seawater and sediments from the Mar Menor lagoon, a hypersaline restricted coastal lagoon in the South East of Spain. Almost half (22) of 50 pharmaceuticals measured were detected, including three anthelmintics (albendazole, levamisole, and thiabendazole. Lagoon concentrations were generally below the limit of quantification (LOQ). LOQs for the three anthelmintics were 0.2, 2.5, and 1.9 ngL^{-1}, while the limit of detection (LODs) were 0.05, 0.8, and 0.6 ngL⁻1, respectively. In addition, albendazole was also one of the fourteen pharmaceuticals detected at the sampling point sited in the Mediterranean Sea used as an external reference. However, its concentration was below the limit of quantification. Thiabendazole was detected in a large number of sediments' samples (83%), but its low extraction recovery limited its evaluation.

Analysis of antibiotic occurrence and fate in water treatment systems continued in the 2015 literature. Fluoroquinolone antibiotics in wastewater influent and receiving waters was the focus of a study by He et al. (2015), who found influent concentrations as high as 1900 ng/L of ciprofloxacin in Maryland wastewater effluent, a concentration in the range of E. coli inhibition. Yan et al (2015) found that fluoroquinolones were detected in 100% of samples collected and removal efficiencies were approximately 65% and were positively correlated with phosphorus removal. This was higher than the treatment efficiencies of 14 different emerging contaminants in two wastewater plants in China at 54 and 48 %.

Transformation Products

A major knowledge gap in the current understanding of emerging contaminants in the environment is the study of transformation products (TPs), or metabolites, of parent compounds which are typically better characterized. The occurrence of transformation products was reviewed by Evgenidou et al. (2015) where they concluded that a scarcity of data exists even for the identification of many groups of chemicals. Furthermore, information on removal efficiencies in wastewater treatment plants (WWTPs) and toxicological data on the effects of these TPs are very poor. In general, research published in 2015 and antibiotics are increasingly incorporated into the study of transformation products and metabolites into experimental methods and design.

Blair et al. (2015) followed pharmaceutical fate in a wastewater treatment system, showing that degradation rates were concentration dependent, slowing as the concentrations decreased, and that for some compounds, negative mass balances existed that could not be explained from sludge-water partitioning. On the other end of water treatment, drinking water represents a direct PCPP-human exposure rout as well as a point of environmental monitoring. Simizake et al. (2015) monitored 64 PCPPs and metabolites in source waters and finished drinking water. They found that although 7 compounds were still detected in finished water, risk of human exposure was negligible and that advanced treatment options (ozonation and granular activated carbon filtration) were more effective in removing these contaminants. This is in agreement with Cai et al. (2015) who showed removal efficiencies between 81–99 % for most PCPPs.

Environmental Risk

Multi-criteria decision analysis was employed along with geologic information systems (GIS) to develop risk maps for antibiotic contamination in the Marmara region of Turkey Kucukdogan et al. (2015). Using hydrologic tools, topography and hydrodynamics, combined with exposure modelling incorporating physicochemical properties that influence fate behavior of antibiotics allowed researchers to identify specific areas of high level risk.

While a majority of the concern regarding trace level antibiotic exposure in the environment centers around human or ecological health and the proliferation of antibiotic resistance, nitrate and nitrous oxide flux was shown to be another sensitive endpoint affected by environmental antibiotic occurrence DeVries et al. (2015). Incubation and column transport studies revealed that the presence of three antibiotics (sulfamethoxazole, narasin, and sulfadiazine) can both inhibit and stimulate denitrification under anaerobic soil conditions at ultra-low levels (ng/kg). The effects of vancomycin in river sediment showed that while microbial community composition changed, nitrate reduction rates overall were unchanged (Laverman et al. (2015)).

Further evaluation of the exposure risk to humans was conducted by Prosser and Sibley, (2015a) who reviewed literature on the uptake of pharmaceuticals in edible portions of plants. From this data, they estimated daily intake for adults and toddlers and compared them to acceptable daily intake levels to identify specific compounds that pose a risk to human health. While their study showed that individually, the human health risk of a single compound is minimal, the accumulated effects of a mixture of compounds could potentially present a hazard and they recommend increased study of mixture toxicity. Further discussion of the work provided by Malchi et al. (2015) and addressed later by Prosser and Sibley (2015b) emphasize the need for additional study on the issue of antibiotic uptake. Gavrilescu et al. (2015) provided a literature review that focused on advances in biomonitoring, ecological risk assessment and advances in bioremediation. They propose that a synergistic approach should be used in research development that furthers knowledge of fate and bioavailability while identifying appropriate means of bioremediation. Another important review was conducted by Clark and Cummings (2015), where both emerging contaminants including PCPPs as well as classic contaminants (persistent organic pollutants POPs) in agricultural fields from biosolid amendments were evaluated. Their work highlights a number of risk assessment strategies that have described.

Wagil et al. (2015) evaluated the ecotoxicity of two anthelmintic drugs (fenbendazole–FEN and flubendazole–FLU) towards different aquatic organisms: luminescent marine bacteria (*Vibrio fischeri*), lumnic inicellular green algae (*Scenedesmus vacuolatus*), duckweed (*Lemna minor*) and crustacean (*Daphnia magna*). *Daphnia magna* appeared to be the most sensitive organism with EC_{50} values for FLU and FEN of 45 μg/L and 19 μg/L, respectively. At environmental concentrations of micrograms per liter, FLU and FEN can impact these organisms in the ecosystem. No adverse effect of FLU and FEN was observed on *Lemna minor.*

Gao et al. (2015) investigated the potential effects of albendazole (ABZ) on the reproduction of earthworms (*Eisenia fetida*). The results demonstrated that ABZ significantly affected the

reproduction of adult earthworms, while survival and growth of adult earthworms were not affected for all ABZ exposed groups. In response to low concentrations of ABZ, cocoon number was more sensitive than other reproductive parameters (cocoon weight, cocoon hatching success and hatching survival, biomass of juveniles and cocoons) during initial 28 d of exposure, showing a significant decrease at 3 mg/kg and above.

The potential health risk for aquatic organisms and humans related to the most frequently used pharmaceuticals in China (the compounds with annual yield of more than 100 tons/year) was estimated by Chen et al. (2015) using two environmental risk assessment methods. The risk quotient (RQ) was estimated using the lowest available toxicity data and an appropriate assessment factor. RQ greater than 1 indicates a risk in aquatic environment. Approximately 90 pharmaceutical compounds, including two anthelmintic drugs (levamisole and niclosamide), were investigated during the study. Niclosamide showed high predicted environmental concentration (10 μg/L) and high risk quotient (RQ = 50.00), while levamisole had low predicted environmental concentration (0.750 μg/L) and limited risk quotient (RQ =0.75).

ANTIBIOTIC RESISTANCE: DRUGS, BUGS, AND GENES

The interconnectedness between the occurrence of antibiotics and corresponding prevalence of antibiotic resistant bacteria and antibiotic resistance genes (ARGs) has long been recognized. Many studies conducted in 2015 examined the concomitance of these ECs. The spread of antibiotics and ARGs from animal farms to adjacent environment via airborne particulate matter (PM) was demonstrated by McEachran et al. (2015). Concentrations as high as 0.5 to 4.6 μg g^{-1} antibiotics (i.e., chlortetracycline, monensin, oxytetracycline, tetracycline, and tylosin) were found in PM in the air immediately downwind of beef cattle feed yards. Genes encoding resistance to tetracycline antibiotics were usually 3 orders of magnitude higher in PM collected downwind of feed yards than in PM collected upwind. Altogether, the work suggests airborne PM as an important route of the dissemination of antibiotic resistance around livestock facilities.

In another study, ARG *sul*(1), *sul*(2), *erm*(A) and *erm*(B) were detected in 70 soil samples collected from 7 dairy farms with relative abundance ranged from 10^{-6} to 10^{-4} copies/16S rRNA gene Sun et al. (2015). The concentrations of major organic pollutants (sulfadiazine, roxithromycin, phenanthrene and pentachlorophenol) were measured at up to 2.9 mg kg^{-1}, with the bioaccessible fraction accounting for 1% to 50% of the total concentrations. Furthermore, the authors found that the abundance of ARGs was positively correlated with the concentrations of the bioaccessible portion of the organic pollutants. Given the common mechanisms of resistance to toxic compounds, such as efflux pumps, the authors hypothesized that the bioaccessible portion of toxic polycyclic aromatic hydrocarbons in soil might have exerted selection pressure that favored bacteria containing resistance genes.

Wang et al. (2015a) determined the fate of ARGs in manure-amended soil as well as the vegetables grown in the soil. A field received manure 5 days before lettuce and endive were planted. Plants were harvested at 30 and 60 days, and then soil and plants samples were analyzed for AB and/or ARGs. Tetracyclines and quinolones were detected in initial soil

samples at the level of 400–500 μg kg^{-1} and 28–32 μg kg^{-1}, respectively, and showed no significant reduction throughout the experiment. Multiple tetracycline and sulfonamide resistance genes were detected in soil (10^{-5} – 10^{-2} copies per copy of the16S rRNA gene) and plant, but none of ARGs encoding resistance mechanisms for beta lactmase, quinolone or erythromycin were detected. Furthermore, the ARG detection frequency in leaf endophyte samples was generally lower than root endophyte samples and phyllosphere samples.

Composting and the use of lagoons are two commonly used methods to treat livestock manure. Wang et al. (2015b) evaluated the effectiveness of these two methods in removing ARB from raw swine manure. Bacteria resistant to erythromycin and tetracycline were quantified using culture-based methods. After 48 days of treatment, erythromycin resistant bacteria were reduced from approximately 7 log to 3 log CFU/g sample by composting and to 6 log CFU/g sample in lagoons. Similarly, tetracycline resistant bacteria were reduced from 8 log to 1 log CFU/g sample by composting and to 6 log CFU/g sample in lagoons. The authors attributed the high removal efficiency of composting to a combination of high temperature, low moisture, limited bacterial mobility, and high enzymatic activities.

In another study, a laboratory experiment was conducted to determine the fate of quinolone resistance genes in manure treated soil Xiong et al. (2015). Manure spiked with fluoroquinolones was incorporated into soils collected from farmlands with manure application history. The amended soils and control soils receiving no manure were then incubated at 20°C in dark, and were sampled at day 0, 30 and 60. Results showed that manure amendment raised the levels of resistance genes (i.e., *oqxA*, *oqxB*, *aac(6′)-Ib-cr* and *qnrS*) in soil 4~100 times. However, the relative abundance of ARGs in manured soil dropped dramatically over a 60-day period after amendment and some genes even dropped to a level lower than that in the control soils. Furthermore, slow removal of ARGs in soil amended with fluoroquinolones-spiked manure suggested the selective pressure exerted by antibiotics could impede the dissipation of the corresponding resistance genes.

Ross and Topp (2015) quantified the abundance of ARGs (i.e., *strA*, *strB*, *sul1* and *aadA*) in bacterial DNA and bacteriophage DNA that were recovered from agricultural soils receiving either dairy manure or municipal biosolids as fertilizer. Generally, after the land application of dairy manure or biosolids, the absolute abundance of ARGs in bacterial DNA increased first before decreasing. The absolute abundance of ARGs in bacteriophage DNA did not vary significantly with time. In addition, it was demonstrated that the presence of bacteriophage in conjunction with selection pressure of antibiotics led to elevated antibiotic resistance of soil bacteria, likely resulting from the transfer of ARGs from bacteriophage to soil bacteria via transduction.

The long-term impacts of manure application on the prevalence of both antibiotics and ARG in paddy soils growing rice were recently assessed by Tang et al. (2015). This study included four field sites; each treatment plot received manure regularly applied for 9 to 30 years while control plots that had received no manure. Tetracyclines were more frequently detected and at higher levels in the top soils of the treated fields than in top soils of the control field. Sulfonamides were also tested but were undetectable in either control or treated fields. In general, tetracycline- and sulfonamide-resistance genes were significantly more abundance

in manure-amended soils than in the control soils. Therefore, long-term application of manure can lead to elevated levels of tetracyclines and ARGs in the top soils in rice paddy soils.

Ferro et al. (2015) demonstrated that the combination of sunlight and hydrogen peroxide treatment could effectively reduce resistant bacteria (*E. coli* and *E. faecalis*) from 10^5 CFU mL^{-1} to below the detection limit (i.e., 2 CFU mL^{-1}) (2015). Consequently, no antibiotic resistant bacteria was detected in top soil or lettuce after being irrigated for 5 weeks using pretreated irrigation water. Similarly, the antibiotic flumequine decreased from 100 to 5.5 μg/L during the pretreatment and did not accumulate in top soil or lettuce following 5-week of irrigation. However, the sunlight plus peroxide treatment was ineffective in degrading carbamazepine and thiabendazole (12% and 50% removal efficiency, respectively), and continuous application of the resulting water lead to antibiotic accumulation in top soil (472 and 256 ng/g, respectively) and lettuce (109 and 18 ng/g, respectively).

Ye et al. (2015) evaluated the effectiveness of biochar amendment in mitigating antibiotic and ARG contamination during lettuce production. Soil containing 12 mg/kg of sulfonamide antibiotics was mixed with biochar derived from thermochemically decomposed maize straw (0.5%, w/w) before lettuce was planted. The authors monitored the levels of sulfonamides and *sul* genes associated with soil and lettuce. Results showed that sulfonamide concentrations decreased at higher rate in soil with biochar compared to soil without biochar (i.e., 94% vs. ~33% removal after 100 days). The authors attributed this to elevated chemical and biological activities in amended soil due to the large specific surface area of and nutrients in biochar. Furthermore, biochar addition resulted in 1 to 2 log reduction of *sul* gene accumulation in lettuce tissues.

A study conducted by Frey et al. (2015) applied liquid swine manure obtained from a farm with antibiotic use history on field plots with tile drainage structures 2 days before precipitation. Tylosin, tetracyclines, and their transformation products, as well as tetracycline resistance gene *tet*(O) were monitored in tile effluent and groundwater water from the experiment site. Peak concentrations of most antibiotics in tile effluent were at the magnitude of 10^2 ng/L. The total antibiotic mass transported through tile effluent was 0.2% of the total antibiotic mass in the manure initially applied to the field. Antibiotics detected in groundwater beneath the field were usually lower than 40 ng/L. In comparison, *tet*(O) in tile effluent and groundwater following the week after manure application increased from no more than 10^1 copies per100 mL to 10^4 and 10^3 copies per 100 mL, respectively.

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