Sulfonamides in the environment: a review and a case report

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ABSTRACT: Sulfonamides are widely used in treatment of animals and humans but pose a risk as environmental pollutants. An analysis of 1588 publications focused on sulfonamides is presented here. The review deals with environmental pollution with sulfonamides, described in papers indexed in the database Web of Science from 1938 to 2011. More in depth details are presented regarding publication activity during the last ten years in which 1255 papers have been published by authors from 1100 institutions. Papers, published during the last three years and mainly in 2011, are listed in comprehensive tables, sorted according to five criteria: reviews, contaminated niches, risk of contamination, sulfonamide transformation and methods of analysis. Key words and shortened abstracts direct the reader to the topics of interest. Hyperlinks to full papers, published in open access journals, are another aid in knowledge dissemination. This design of the review article allows easy navigation through vast amounts of information. Finally, a case report illustrates experiences from the author's laboratory with sulfamethazine determination in pig slurry by ELISA. The reported results highlight the need for updating the legal directives for environmental protection.

Keywords: sulfonamides; sulfamethazine; sulfamethoxazole; environmental protection; bacterial resistance; pig slurry; novel review design

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1. Introduction

Sulfonamides are frequently used in pigs and cattle for the treatment of bacterial diseases. Therefore, pig and cattle farms pose a risk for the contamination of soil and surface water with sulfonamides and other antibiotics. This is a good reason for intensive research into sulfonamides, which covers their detection, distribution, transformation, and impact on microorganisms in the surrounding environment, the development of resistance of microorganisms to sulfonamides, and the possible harmful effects on the treatment of animal and human bacterial diseases. Sulfonamides are unacceptable contaminants of food, which is an another reason for the development and introduction of different methods for sulfonamide detection in animal excrements, slurry, liquid dung, sewage water, soil, surface and ground water, and in foodstuffs and animal tissues. This review is not an exhaustive presentation of the current data. Instead, the aim is to highlight the need for improving current technologies for animal production from the point of view of environmental protection, food and water safety and human health protection. There is no doubt that residues of pharmaceutical drugs, sulfonamides included, are only one element of the multiple risk factors, concerning modern industry and advanced technology. Data that we consider as important are presented in tables with source citations and a few descriptive words. The tables comprise only the most important publications from the period of the last three years with an emphasis on papers published in 2011. Publications included in this review are sorted according to five criteria (reviews, contaminated niches, risk of contamination, sulfonamide transformation and methods for analysis). References in the tables are described using a few words and are supplemented by full or shortened abstracts. The List of References, completed by hyperlinks to the full text of many of the cited articles (published in open access journals) is available for readers on e-mail request. This novel review design allows the easy selection of information required by readers according to their needs and facilitates efficient knowledge dissemination.

Our own experiences of screening for sulfonamide repeatedly in pig slurry from four farms by ELISA are appended as a case report in part 3 of this article.

2. Review

2.1. Database used as the source of information

The Web of Science® database (Thomson Reuters, New York, USA) includes publications from over 12 000 of the highest impact journals. Records have been retrieved using the following search profile:

Topic = (sulfonamide*AND (manure OR feaces OR slurry OR dung OR water OR environment*))

Timespan = all years or 2002–2011

Databases = SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, CCR-EXPANDED, IC.

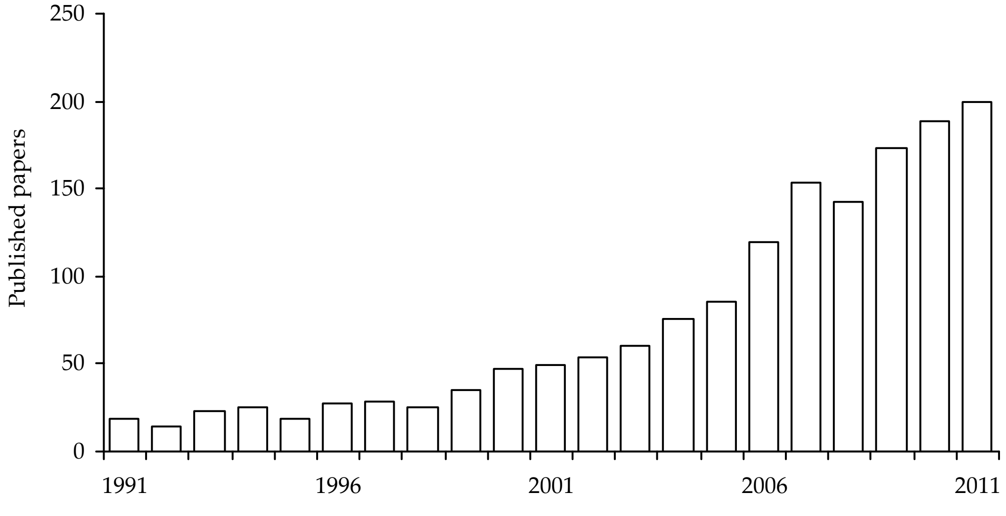

Figure 1. Papers on sulfonamides in the environment, published in journals indexed in the Web of Science database (1567 papers have been indexed from 1991 to 2011)

In addition to comprehensive coverage, the Web of Science database (WOS) provide users with the option of searching by cited references and by citing papers lists with links to the records of all papers published in the journals indexed in WOS. Moreover, a quick and easy analysis of search results according to authors, institutions, countries, sources (journals), year of publication, author identification, journals characteristics, impact factor, etc., is possible.

2.2. Basic analysis of publications on sulfonamides in the environment

The search using the above mentioned profile (see 2.1, Topic =) resulted in the retrieval of 1588 records. Twenty one papers have been published from 1938 to 1990. The number of published papers progressively increased in the years from 1991 to 2011 when 1567 papers were published (Figure 1). Two hundred papers were published in 2011.

During the last ten years 1255 papers have been published. Original papers (articles) comprised 94.4% of this number. The articles have been published in 385 journals by 3845 authors residing in 69 countries and affiliated to 1100 institutions. The most productive authors, institutions and countries (Top 10) are presented in Table 1. Journals, which in the last ten years have published more than 20 papers (more than 1.5% of the total) are listed in Table 2.

Table 1. The most productive authors, institutions and countries with regard to publications on sulfonamide in the environment (Web of Science, 1255 papers indexed from 2002 to 2011)

Item	Number of papers
Authors (3845 in total)	
Supuran CT	52
Scozzafava A	39
Barcelo D	17
Ebinghaus R	16
Jones PG	16
Blaschette A	15
Thiele-bruhn S	15
Moers O	14
Ahrens L	13
Innocenti A	13
Institutions (1100 in total)	
University Florence	51
Chinese Academy of Sciences	46
University Valencia	25
Environment Canada	21
Colorado State University	19
Nankai University	18
Technical University Carolo-Wilhelmina, Braunschweig	18
University Roma La Sapienza	16
University Toronto	16
CSIC (Consejo Superior de Investigaciones Cientificas, Spain)	14
US Geological Survey	14
Countries (69 in total)	
USA	251
P.R. China	189
Germany	156
Spain	110
Italy	91
Canada	84
Japan	70
India	42
England	41
France	34
Switzerland	34

2.3. Important review articles published in recent years

Review articles, published in 2009, 2010 and 2011, are presented in Table 3. All important topics are covered, e.g., general information on common types of sulfonamides polluting the environment (Baran et al. 2011; Zhang and Li 2011), sample preparation (Namera et al. 2011; Samanidou and Karageorgou 2011), and analytical methods used for sulfonamide detection, namely HPLC (Seifrtova et al. 2009; Tolika et al. 2010), capillary electrophoresis (Garcia-Campana et al. 2009; Pinero et al. 2011), and immunoassays (Nesterenko et al. 2009). Some reviews deal with resistance (Le-Minh et al. 2010; Jury et al. 2011), or the degradation of different pollutants, sulfonamides included (Sharma 2010). The same topics can be found also in original papers, presented in Tables 4 to 7 (topics in the left column, abstracts in the middle).

Table 2. Journals with the most papers on sulfonamides in the environment (Web of Science, 1255 papers indexed from 2002 to 2011, journals in total 385)

Item	Number of papers
Journal of Chromatography A	76 (6.1%)
Environmental Science Technology	65 (5.2%)
Chemosphere	52 (4.1%)
Journal of Agricultural and Food Chemistry	39 (3.1%)
Analytical and Bioanalytical Chemistry	34 (2.7%)
Analytica Chimica Acta	28 (2.2%)
Bioorganic Medicinal Chemistry Letters	28 (2.2%)
Science of the Total Environment	22 (1.8%)
Zeitschrift fur Anorganische und Allgemeine Chemie	22 (1.8%)
Water Research	21 (1.7%)

2.4. Main sources of soil and water contamination by sulfonamides: pig and cattle manure, slurry and liquid dung, hospital waste water and sewage

Contamination of the environment, mainly soil and surface water, is a worldwide problem. Pharmaceuticals, used for the treatment of cattle and pigs in large scale units are excreted by animals into manure or liquid dung and in this way kilograms of drugs can be transfered to fields under cultivation or pasture. Part of the pollutants is absorbed to the soil, while another portion is flushed by rain water into the draining system and finally into surface water. The environmental load may be very serious. Many different factors, often variable over time, play a role. The most important factors determining the intensity of environmental contamination are the following: number of animals in the facility, requirements for their treatment, drugs used for treatment, the technology used for fertilization, field surface, soil type, weather, etc. The highest concentrations are reported in animal and hospital sewage waters and near reservoirs outlets. Sulfamethazine and sulfamethoxazole are preferred for the treatment of animals and humans, respectively. Seventeen papers (12 of them published in 2011) are presented in Table 4. Two older publications should not be omitted if interest is focused on sulfonamides in the environment as veterinary drugs and one wishes to obtain a global perspective on the use, sales, exposure pathways, occurrence, fate and effects of veterinary antibiotics in the environment (Sarmah et al. 2006; Sukul and Spiteller 2006).

2.5. The risk posed by sulfonamides in soil and water

Twelve papers published in 2011 have further supported the body of literature indicating that sulfonamides and other antimicrobial drugs are present in high concentrations and pose a real risk not only by inducing bacterial resistance but also by a direct impact on bacteria and plants. Selected papers published from 2009 to 2011 on this topic are presented in Table 5. Sulfonamides affect soil microorganisms, which have an important role in many soil functions and plant physiology. Antibiotic resistance genes are studied most commonly in *E. coli* isolated from soil and water contaminated with antibacterial drugs (Graves et al. 2011; Karczmarczyk et al. 2011; Persoons et al. 2011). A dose-dependent effect of sulfadiazine on the soil microbial community and microbial biomass has been described (Hammesfahr et al. 2011), and the toxicity of the products of the electrochemical oxidation of sulfamethoxazol on the marine bacterium *Vibrio fischeri* has been demonstrated (Dirany et al. 2011). Screening for the phytotoxicity of antibiotics revealed that sulfamethoxazole belongs to the most potent antibiotics and that carrot is the most sensitive plant species (Hillis et al. 2011).

2.6. Movement and transformation of sulfonamides in soil and water

The technology of manure or dung use and distribution and the responsibilities of farm managers to the workers handling manure, which represents both a valuable fertilizer and a dangerous waste product, is an area which should receive critical attention. Consideration should be given to possible harmful effects, not only indirect ones such as medical problems arising from the treatment of infections due to resistant bacteria, but also direct losses on a plant and in animal production on the farm in question. Therefore, both legal directives for the use of antibiotics and knowledge dissemination among farm managers, veterinarians and ecologists should be constantly reviewed and under the control of state authorities. Recent research has focused on the movement of pollutants in the environment and their degradation and transformation. Fifteen papers addressing these issues published in 2011 are presented in Table 6.

2.7. The most frequently used methods for sulfonamide detection

All the aforementioned efforts are inconceivable without analytical methods for sulfonamide detection and financial resources for their development, validation and application. An inseparable part of the whole problem is a sound legal base for the directives used to treat infections in humans and animals and the most effective waste management with respect to all aspects of the problem, e.g., health, food production and consumer and environmental protection. Very sophisticated, precise, accurate and reliable instrumental methods are available together with relatively simple and fast methods, which are suitable for large scale procedures performed preferably in a well equipped laboratory or applicable on site and giving results within minutes. Both sets of techniques should be utilized with a good understanding of their respective advantages and disadvantages and without any prejudice because the methods should not be in competition. The only criteria for their application must be that the deliver the correct answer in the right place with acceptable costs. There is no doubt that both high tech instrumentation and the most current knowledge on the application of bioassays and nanotechnology must be taken into account. Papers on sulfonamide analysis, published from 2009 to 2011 are presented in Table 7 (32 articles, 19 published in 2011). Described therein are advances in sample preparation, solid and solvent extraction, microwave-assisted extraction, precolumn derivatization, multiclass and multiresidue methods, new protocols for high performance liquid chromatography coupled to tandem mass spectrometry (HPLC-MS/MS), liquid chromatography with fluorometric and UV detection and diode array, capillary electrophoresis, immunochemical methods, ELISA, immunochromatography, biosensors, flow injection with a novel potenciometric design, differential pulse voltammetry with overoxidized polypyrrole modified pencil graphite electrodes, etc. For details on new publications see Table 7. Our older review discusses antibody-based methods for environmental and food analysis (Franek and Hruska 2005).

3. Case report

3.1. Sulfonamide presence in pig slurry shown by ELISA

An ELISA method developed using a sensitive polyclonal antibody (Franek et al. 1999), was used to screen for sulfonamides in the slurry of four pig farms. Sampling was carried out once from ten sampling places on three farms and repeatedly from eight sampling places on two farms. The liquid dung was mixed in the reservoir, if possible, using the available technology, or two samples were collected from different places and then combined. ELISA was performed in duplicate or triplicate. The results are presented in Figure 2. The first run of sampling revealed high sulfamethazine concentrations in two sampling places on Farm 3; these then gradually decreased in the second and third runs of sampling. A similar trend was observed in another sampling place on the same farm; however, concentrations were below 50 μg/kg. Nevertheless, this is strong evidence that the ELISA is reliable even at very low concentrations of sulfamethazine. The samples of slurry from two farms (Farm 1 and Farm 2) were sulfamethazine-free in the first sampling and were not assessed further. A contamination higher than 50 μg/kg was found on Farm 4 in one sampling place during the first sampling and in

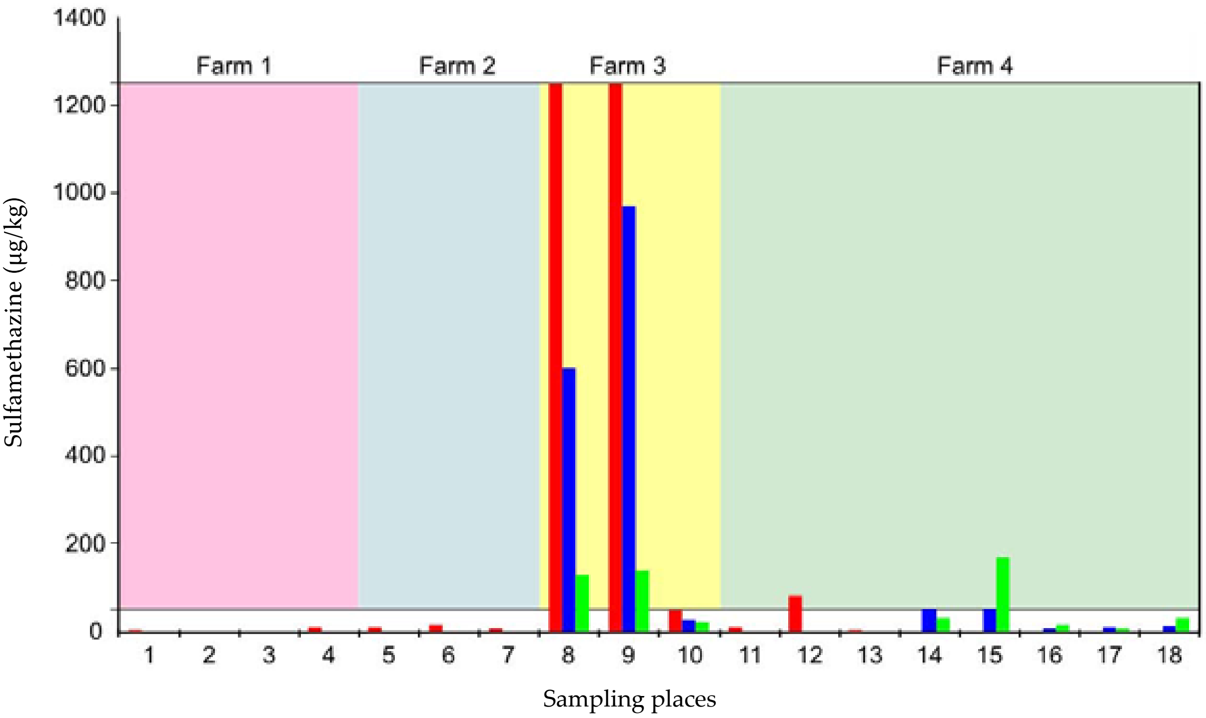

Figure 2. Screening for sulfamethazine in pig slurry by ELISA (Franek et al., 1999). Farm 1 = sampling places 1 to 4; Farm 2 = sampling places 5 to 7; Farm 3 = sampling places 8 to 10; Farm 4 = sampling places 11 to 18. Red columns = sampling in February; blue columns = sampling in May; green columns = sampling in June

another place during the third sampling. A very low contamination of liquid dung from five sampling places was found in the samples, taken in the second and third run.

The same method was also used to detect sulfamethazine in the water and sediment from a stream near Farm 3. Negligible concentrations have been found, but the water was analyzed only once and a year later the slurry was shown to be positive. Moreover, it was not possible to take into account the effect of the application of dung as a fertilizer. Nevertheless, small differences between the replicates and the appropriate values determined in spiked water and sediment allow us to consider the ELISA suitable for the screening of sulfamethazine contamination.

In summary, although the use of sulfonamides as chemotherapeutics is not prohibited, environmental protection should be strictly enforced by appropriate legal measures which are unfortunately not yet in force. Environmental protection authorities should have the right to analyse samples of manure or slurry from reservoirs on farms, and should be informed when, where and how the manure has been used. According to the geographical configuration the sampling of surface water and sediment from a catchment should be scheduled so as to ensure permanent periodical checks. This inspection should also cover antibiotics, pesticides and known zoonotic microorganisms, including mycobacteria in dairy and cattle farms. The inspectors should be supplied with standard operation protocols for sampling and data collection and accredited laboratories should be provided with methods for the detection of key pollutants.

4. Acknowledgements

Sampling of pig slurry and surface water was carried out by Mgr. M. Kostka, University of South Bohemia, Ceske Budejovice and sulfonamide detection by Dr. Iva Diblikova, Veterinary Research Institute, Brno. These two individuals generated the data presented in part 3 of this paper and their technical assistance is greatly appreciated.

Table 3. Important review articles: key words and extracts from abstracts

REVIEWS		
Resistance **Seveage plants**	Examination of available literature suggests that relative levels of antibiotic resistance may be increased during sewage treatment processes. However, it is unclear whether this may be partially the result of horizontal gene transfer or entirely due to clonal propagation. While there is circumstantial evidence that the presence of antibiotics or other related genetic promoters in STP wastewaters may contribute to selective pressures for these processes, a definite role is yet to be demonstrated.	Jury et al. 2011
Monolith **Sample preparation** **Devices**	Monolith has been modified to suit various devices for the extraction and enrichment of analytes in any matrices of environmental, food, and biological analyses. This approach has contributed to miniaturization and automation for sample preparation, and it can reduce the time and cost requirements of sample preparation. Recently, numerous applications have been demonstrated for online and inline preconcentration coupled with monolith, and many kinds of devices have been designed and developed for offline devices.	Namera et al. 2011
General impact	This review presents the most common types of sulfonamides used in healthcare and veterinary medicine and discusses the problems connected with their presence in the biosphere. These drugs have caused changes in the population of microbes that could be potentially hazardous to human health. This human health hazard could have a global range, and administrative activities have been ineffective in risk reduction.	Baran et al. 2011
Capillary electrophoresis	CE is popular due to its simplicity, speed, highly efficient separations and minimal solvent and reagent consumption; it can also be included as a useful technique in the nanotechnology field and it covers a wide range of specific applications in different fields (chemical, pharmaceutical, genetic, clinical, food and environmental). However, this technique is still not well accepted in routine laboratories for food analysis. Although these papers frequently prove the potential of this methodology in spiked samples, it is not common to find a discussion of the well-known complexity of the matrices to extract analytes from the sample and/or to study the interferences in the target analytes.	Pinero et al. 2011
Separation **Sample preparation**	Monolithic columns with a unique structure possess some exceptional characteristics, which make them an excellent tool in the hands of analytical chemists, not only for separation but also for sample preparation. Their much higher external porosity compared to conventional particle-packed columns results in higher permeability and low-pressure drop with higher separation efficiency. Till now, monolithic columns have been applied to the analysis of different analytical matrices: pharmaceuticals, biofluids, food matrices, environmental samples, biochemical species, proteomics, etc.	Samanidou and Karageorgou 2011
General results	The authors summarized the latest information on occurrence, transformation, and fate of antibiotics in WWTPs based on more than 90 papers published in the past eight years. The results show that extensive researches on antibiotics occurrence have been conducted mainly in East Asia, North America, Europe, and Australia. Adsorption, biodegradation, disinfection, and membrane separation were the dominant removal routes for antibiotic in different wastewater treatment processes of WWTPs. Many antibiotics cannot be removed completely in wastewater treatment processes and would enter into environment via effluent and sludge.	Zhang and Li 2011
Pollutants degradation **Ferrate(VI) technology**	A novel ferrate(VI) technology can treat a wide range of pollutants and microorganisms in water and wastewater. The aim of this paper is to review the kinetics and products of the oxidation of nitrogen-containing inorganic (ammonia, hydroxylamine, hydrazine, and azide) and organic (amines, amino acids, anilines, sulfonamides, macrolides, and dyes) compounds by ferrate(VI) in order to demonstrate the feasibility of ferrate(VI) treatment of polluted waters of various origins. Several of the compounds can degraded in seconds to minutes by ferrate(VI) with the formation of non-hazardous products.	Sharma 2010

REVIEWS		
Water recycling **Bacterial resistance**	Municipal water recycling processes are potential human and environmental exposure routes for low concentrations of persistent antibiotics. While the implications of such exposure scenarios are unknown, concerns have been raised regarding the possibility that continuous discharge of antibiotics to the environment may facilitate the development or proliferation of resistant strains of bacteria. As potable and non-potable water recycling schemes are continuously developed, it is imperative to improve our understanding of the fate of antibiotics during conventional and advanced wastewater treatment processes leading to high-quality water reclamation. This review collates existing knowledge with the aim of providing new insight to the influence of a wide range of treatment processes to the ultimate fate of antibiotics during conventional and advanced wastewater treatment. Although conventional biological wastewater treatment processes are effective for the removal of some antibiotics, many have been reported to occur at 10–1000 ng/l concentrations in secondary treated effluents. These include beta-lactams, sulfonamides, trimethoprim, macrolides, fluoroquinolones, and tetracyclines. Tertiary and advanced treatment processes may be required to fully manage environmental and human exposure to these contaminants in water recycling schemes. The effectiveness of a range of processes including tertiary media filtration, ozonation, chlorination, UV irradiation, activated carbon adsorption, and NF/RO filtration has been reviewed and, where possible, semi-quantitative estimations of antibiotics removals have been provided.	Le-Minh et al. 2010
HPLC **Pharmaceutical preparations** **Biological fluids**	HPLC can provide a valuable tool for generating highly pure preparations for characterizing the antimicrobial activities. In the present review article, column and mobile phase conditions as well as sample preparation issues are taken into consideration. A brief discussion on chemical structure, spectrum of activity and action mechanism of sulfonamides has also been provided. The time frame of papers covered by this review article starts at 1974 and ends at 2009.	Tolika et al. 2010
Capillary electrophoresis **Foodstuffs of animal origin** **Environmental samples**	In this paper we review applications of capillary electrophoresis (CE) to the determination of antibiotic residues in food derived from animals and in environmental samples.	Garcia-Campana et al. 2009
Immunoassays	Recent achievements in the detection of sulfanylamide drugs in environmental objects and foodstuffs are considered. These are the specific detection of individual substances; class-specific immunoassay of the whole group of sulfamide drugs; widely used ELISA methods; biosensors; fluorescence polarization immunoassay; and new promising methods for the detection of sulfamide drugs, immunochromatographic test strips, the method using molecularly imprinted polymers, piezoelectric quartz immunosensors, etc.	Nesterenko et al. 2009
Environmental samples **Analytical methods** **HPLC-MS/MS**	An over-view of analytical methodologies for the determination of quinolone (Qs) and fluoroquinolone (FQs), macrolide (MLs). tetracycline (TCs), sulfonamide (SAs) antibiotics and trimethoprim (TMP) in different environmental waters. The analysis of these antibiotics has usually been carried out by high-performance liquid chromatography (HPLC) coupled to mass spectrometry (MS) or tandem mass spectrometry (MS/MS) and to a lesser extent by ultraviolet (UV) or fluorescence detection (FD). A very important step before LC analysis is sample preparation and extraction leading to elimination of interferences and prevention of matrix effect and preconcentration of target analytes.	Seifrtova et al. 2009

Table 4. Main sources of soil and water contamination by sulfonamides: pig and cattle manure, slurry and liquid dung, hospital waste water and sewage

CONTAMINATION		
Aquatic ecosystems, **Canada** **Contamination**	Pharmaceuticals are commonly used in the livestock industry, and studies have demonstrated that some pharmaceuticals can reach receiving water bodies. The main objective of this study was to measure the occurrence and concentration of selected veterinary pharmaceutical compounds commonly used by the livestock industry in Alberta across streams varying in agricultural intensity. A total of 247 water samples were collected from 23 watersheds during the open water season between, May 2005 and May 2006. Samples were analyzed for 27 commonly used veterinary pharmaceuticals from the following compound classes: avermectins, beta lactams, fluoroquinolones, ionophores, lincosamides, macrolides, sulfonamides, and tetracyclines. Subsequently, 10 antimicrobials were detected: narasin, salinomycin, monensin, sulfamethazine, sulfathiazole, sulfadoxine, erythromycin, lincomycin, chlortetracycline, and oxytetracycline. Trace (ng/l) concentrations of antimicrobials were detected in 51% of the samples (127 out of 247 samples). Monensin and sulfamethazine were detected most frequently (34% and 8% of samples, respectively). Monensin concentrations ranged from below the detection limit of 2 ng/l to 843 ng/l. Monensin detection frequencies in study watersheds were correlated to manure production percentiles and regional cattle densities. Monensin concentrations were found to be significantly correlated to several water quality parameters (e.g., NH_3-N). Monensin detection frequencies were found to be significantly higher in the spring than in the fall. Maximum concentrations for the other nine antimicrobials detected ranged between 3 and 250 ng/l. The antimicrobials detected and their concentrations were found to be similar to those in some recent European and North American livestock pharmaceutical stream surveys. Findings from this study can inform future monitoring programs and provides ambient concentrations for environmental (fate and transport) and toxicity studies to better evaluate potential risks to humans and the receiving aquatic ecosystems.	Forrest et al. 2011
Soil, USA **pH** **Soil charge density** **Contact time**	In this research, the mobility of two sulfonamides – sulfamethazine (SMN), sulfathiazole (STZ) and a conservative bromide tracer was investigated in three soils collected from regions in the United States with large number of concentrated animal-feed operations. Results of a series of column studies indicate that the mobility of these two sulfonamides was dependent on pH, soil charge density, and contact time. At low pH and high charge density, substantial retention of sulfonamides was observed in all three soils investigated, due to the increased fraction of cationic and neutral forms of the sulfonamides. Conversely, enhanced mobility was observed at high pH, where the sulfonamides are predominantly in the anionic form. The results indicate that when both SMN and STZ are predominantly in anionic forms, their mobility approximates the mobility of a conservative bromide tracer. This observation is consistent for the mobility of both SMN and STZ individually, and also in the presence of several other antimicrobials in athree soils investigated. Higher contact time indicates lower mobility due to increased interaction with soil material.	Kurwadkar et al. 2011
Soil and manure, Korea **Risk for groundwater**	This study investigated the mobility of veterinary drugs in the soil column with the application of manure compost to assess the risk of groundwater contamination by leaching in the Korean agricultural environment. The degree of sulfonamides and tetracyclines mobility, measured by the concentration of leachates from silty loam soil for nine days, was observed being on the first day of this study, in the order sulfathiazole, sulfamethazine > sulfamethoxazole > chlortetracycline > oxytetracycline, and the sulfonamides concentrations were about ten times higher than the tetracyclines concentrations with continuous leaching. The results indicate that sulfonamides pose a high risk of ground and surface water contamination and tetracyclines have the potential to persist in soils with bioactive epimers.	Kwon 2011 Kwon et al. 2011

CONTAMINATION		
Soil in Pearl River Delta, China **Livestock farms**	Thirteen antibiotics in soil from vegetable farmlands of the Pearl River Delta, southern China, were investigated. At least three antibiotics were detected in each sample. Six antibiotics including four quinolones, tetracycline, and sulfamethoxazole were detected in > 94% of the samples. The total contents of three tetracyclines, eight sulfonamides, and four quinolones were not detected-242.6, 33.3–321.4, and 27.8–1537.4 μg/kg, respectively. The highest antibiotic concentrations were observed mainly in vegetable farmlands affiliated with livestock farms. Chlortetracycline, sulfameter, and quinolones in some samples exceed the ecotoxic effect trigger value (100 μg/kg) set by the Steering Committee of Veterinary International Committee on Harmonization. The composition and concentration of antibiotics in soil were correlated with vegetable species. This study has revealed an alarming condition of antibiotics in vegetable farmland soil. Further investigation including environmental fate, plant uptake, and human exposure to antibiotics by plant-derived food should be conducted.	Li et al. 2011b
Haihe River, China **Water** **Sediments** **Swine farms** **Fishponds**	The occurrence and transport of 12 antibiotics (from the tetracycline, sulfonamide, quinolone, and macrolide families) was studied in a 72-km stretch of the Haihe River, China, and in six of its tributaries. Aqueous and sediment samples were analyzed by HPLC-MS/MS. Sulfonamides were detected at the highest concentrations (24–385 ng/l) and highest frequencies (76–100%). Eight of the 12 antibiotics likely originated from veterinary applications in swine farms and fishponds, and concentrations at these sources (0.12–47 μg/l) were 1–2 orders of magnitude higher than in the effluent of local wastewater treatment plants. Sulfachloropyridazine (SCP) was detected in all swine farm and fishpond samples (maximum concentration 47 μg/l), which suggests its potential usefulness to indicate livestock source pollution in the Haihe River basin. Hydrological and chemical factors that may influence antibiotic distribution in the Haihe River were considered by multiple regression analysis. River flow rate exerted the most significant effect on the first-order attenuation coefficient (K) for sulfonamides, quinolones, and macrolides, with higher flow rates resulting in higher K, probably due to dilution. For tetracyclines, sediment total organic matter and cation exchange capacity exerted a greater impact on K than flow rate, indicating that adsorption to sediments plays an important role in attenuating tetracycline migration. Overall, the predominance of sulfonamides in the Haihe River underscores the need to consider regulating their veterinary use and improving the management and treatment of associated releases.	Luo et al. 2011
Mess River, Luxembourg	Urban and agricultural areas affect the hydraulic patterns as well as the water quality of receiving drainage systems, especially of catchments smaller than 50 km^2. Urban runoff is prone to contamination due to pollutants like pesticides or pharmaceuticals. Agricultural areas are possible sources of nutrient and herbicide contamination for receiving water bodies. The pollution is derived from leaching by subsurface flow, as well as wash-off and erosion caused by surface runoff. In the Luxembourgish Mess River catchment, the pharmaceutical and pesticide concentrations are comparable with those detected by other authors in different river systems worldwide. Some investigated pesticide concentrations infringe current regulations. The maximum allowable concentration for diuron of 1.8 μg/l is exceeded fourfold by measured 7.41 μg/l in a flood event. The load of dissolved pesticides reaching the stream gauge is primarily determined by the amount applied to the surfaces within the catchment area. Storm water runoff from urban areas causes short-lived but high-pollutant concentrations and moderate loads, whereas moderate concentrations and high loads are representative for agricultural inputs to the drainage system. Dissolved herbicides, sulfonamides, tetracyclines, analgesics and hormones can be used as indicators to investigate runoff generation processes, including inputs from anthropogenic sources. The measurements prove that the influence of kinematic wave effects on the relationship between hydrograph and chemographs should not be neglected in smaller basins. The time lag shows that it is not possible to connect analysed substances of defined samples to the corresponding section of the hydrograph.	Meyer et al. 2011

Water, 37 rivers, Japan **Sulfamethazine** **Livestock waste**	We report the results of a nationwide survey of commonly used human and veterinary antibiotics (seven sulfonamides, trimethoprim, and four macrolides) in 37 Japanese rivers. Concentrations of the sum of the 12 target antibiotics ranged from undetectable to 626 ng/l, with a median of 7.3 ng/l for the 37 rivers. Antibiotics concentrations were higher in urban rivers than in rural rivers and were correlated with those of molecular markers of sewage (crotamiton and carbamazepine). Macrolides were dominant over sulfonamides in urban rivers. Sulfonamides, especially sulfamethazine (used in animals), were dominant in a few rivers in whose catchment animal husbandry is active. However, these signals of veterinary antibiotics were overwhelmed by those of human antibiotics in lower reaches of most rivers. The analysis of the antibiotics in all 88 samples showed that the target antibiotics in Japanese rivers are derived mainly from urban sewage, even though larger amounts of antibiotics are used in livestock. Most of the livestock waste-derived antibiotics are unlikely to be readily discharged to surface waters.	Murata et al. 2011
Coastal water, **Yellow Sea, China**	We have therefore developed a method for the rapid detection of 36 antibiotic residues in coastal waters, including tetracyclines (TCs), sulfanilamides (SAs), and quinolones (QLs). The method consists of solid-phase extraction (SPE) and liquid chromatography-tandem mass spectrometry (LC-MS/MS) analysis, using electrospray ionization (ESI) in positive mode. The SPE was performed with Oasis HLB and Oasis MCX cartridges. Chromatographic separation on a C18 column was achieved using a binary eluent containing methanol and water with 0.1% formic acid. Typical recoveries of the analytes ranged from 67.4% to 109.3% at a fortification level of 100 ng/l. The precision of the method, calculated as relative standard deviation (RSD), was below 14.6% for all the compounds. The limits of detection (LODs) varied from 0.45 pg to 7.97 pg. The method was applied to determine the target analytes in coastal waters of the Yellow Sea in Liaoning, China. Among the tested antibiotics, 31 were found in coastal waters, with their concentrations between the LOD and 212.5 ng/l. These data indicate that this method is valid for analysis of antibiotics in coastal waters. The study first reports such a large number of antibiotics along the Yellow Sea coast of Liaoning, and should facilitate future comprehensive evaluation of antibiotics in coastal ecosystems.	Na et al. 2011
Swine manure, **China**	The scientific interest in the occurrence and fate of antibiotics in animal husbandry has increased during the past decades because of the emergence and development of antimicrobial resistance in pathogenic bacteria. This study developed a method for simultaneous detection of five sulfonamides, three tetracyclines and one macrolide in swine manure with stable recoveries (73.0–110.6%) and high sensitivity (limit of quantification < 90 μg/kg. Thereafter, a total of 126 swine manure samples, collected from 21 concentrated animal feeding operations (CAFOs) in Shandong Province of China during summer and winter, were analyzed. The potential influences of different sampling seasons, swine types and food sources on residual antibiotic concentrations were examined in detail. The maximum concentration of residual antibiotic could reach up to 764.4 μg/kg (chlortetracycline), and the detection frequencies were 84.9–96.8% for tetracyclines, 0.8–51.6% for sulfonamides and 4.8% for macrolide. These data reveal that antibiotics were extensively used in CAFOs in this district and the manure may act as a non-specific source of antibiotic residue in farmlands and aquatic environments.	Pan et al. 2011a
Sewage water, **Spain** **Multianaylysis** **(33 analyts)** **SPE, LC/MS-MS**	This paper describes the presence of 33 pharmaceuticals and hormones in waters from two sewage treatment plants (STPs) situated in Catalonia, in northeastern Spain. The target compounds were one psychoactive stimulant, one antiepileptic, four analgesics and non-steroidal anti-inflammatories, one lipid regulators, two anti-ulcer agents, nine antibiotics (sulfonamides and macrolides), two beta-blockers, two metabolites, and 11 hormones (free and conjugates). The determination was performed using liquid chromatography coupled to tandem mass spectrometry after enrichment by solid-phase extraction with Oasis HLB sorbent. Most of the pharmaceuticals were found in both influent and effluent samples from the two STPs. The most frequently detected were caffeine, acetaminophen, carbamazepine, diclofenac, ibuprofen, naproxen, sulfamethoxazole, sulfapyridine, sulfathiazole, ranitidine, omeprazole, estrone 3-sulfate, and estradiol 17-glucuronide. Specifically, the highest concentrations found in influents were 19 850 ng/l (acetaminophen), 9945 ng/l (caffeine), 4215 ng/l (ibuprofen), 5695 ng/l (sulfamethoxazole), and 5140 ng/l (sulfathiazole). Most of the pharmaceuticals present in influent waters were found in effluents at lower concentrations. The highest concentrations in effluents were 970 ng/l (caffeine), 670 ng/l (sulfamethoxazole), 510 ng/l (bezafibrate), and 1032 ng/l (diclofenac).	Pedrouzo et al. 2011

CONTAMINATION		
Pearl River, China	Occurrence, behavior and fate of several groups of antibacterials were investigated in municipal wastewater, sewage sludge, and urban river water in China. Fluoroquinolones (e. g., ciprofloxacin, norfloxacin, and ofloxacin), macrolides (dehydroerythromycin, roxithromycin, and clarithromycin), sulfonamides (sulfamethoxazole and sulfamethazine) and trimethoprim were ubiquitously detected in the wastewater in China. Fluoroquinolones were generally the most abundant in the raw sewage, with a maximum concentration of up to 6415 ng/l observed for norfloxacin. Sulfonamides and macrolides transported predominantly in the aqueous phase. A median percentage of 67% of sulfonamides and 86% of macrolides remained in the final effluent after treatment in sewage treatment plants. On the contrary, sorption played a significant role in transport of fluoroquinolones and approximately half of the fluoroquinolones finally ended up and persisted in the dewatered sludge. In the urban section of the Pearl River at Guangzhou, sulfonamides, trimethoprim, and macrolides were widely present at median concentrations of 22–735 ng/l, whereas fluoroquinolones were only occasionally detected at 2–152 ng/l, probably due to their strong tendency of partition to sediment and/or photodegradability. The result of principal components analysis suggests input of non-sewage derived sulfamethazine in the Pearl River. Seasonal variations of the antibacterials distribution in the wastewater are mainly ascribed to different consumption. Dilution effect by precipitation, however, also plays an important role in seasonal distribution of the antibacterials in the Pearl River.	Peng et al. 2011
Animal wastewater **Surface water, China** **HPLC/ESI-MS/MS**	The objective of this investigation was to obtain a broad profile of veterinary antibiotics residues in animal wastewater and surface water around large-scale livestock and poultry farms in Jiangsu Province of China. Therefore, 53 samples collected from 27 large-scale animal farms in 11 cities and counties of Jiangsu Province in 2009 were monitored for 10 selected veterinary antibiotics using solid phase extraction and high performance liquid chromatography/electrospray ionization-tandem mass spectrometry (HPLC/ESI-MS/MS) techniques. Ten veterinary antibiotics were found in animal wastewaters, eight antibiotics were detected in pond waters, and animal farm-effluents and river water samples were contaminated by nine antibiotics. The most frequently detected antibiotics were sulfamethazine (75%), oxytetracycline (64%), tetracycline (60%), sulfadiazine (55%) and sulfamethoxazole (51%) which were detected with a maximum concentration of 211, 72.9, 10.3, 17.0 and 63.6 μg/l, respectively. The maximum concentration of 0.55 μg/l for cyromazine, 3.67 μg/l for chlortetracycline, 0.63 μg/l for sulfadoxine, 39.5 μg/l for doxycycline and 0.64 μg/l for sulfaquinoxaline were determined in the collected samples. In general, the maximum concentration of the selected veterinary antibiotics was detected in animal wastewaters except for chlortetracycline in animal farm-effluents. In addition, residue levels of selected veterinary antibiotics in animal wastewater and surface water around the farms were related to animal species and have a high spatial variation.	Wei et al. 2011
Dairy farm **Surfaces** **Manure collection systems** **Soil** **Shallow groundwater**	Environmental releases of antibiotics from concentrated animal feeding operations (CAFOs) are of increasing regulatory concern. On two dairies we conducted four seasonal sampling campaigns, each across 13 animal production and waste management systems and associated environmental pathways: application to animals, excretion to surfaces, manure collection systems, soils, and shallow groundwater. Concentrations of antibiotics were determined using on line solid phase extraction (OLSPE) and liquid chromatography-tandem mass spectrometry (LC/MS/MS) with electrospray ionization (ESI) for water samples, and accelerated solvent extraction (ASE) LC/MS/MS with ESI for solid samples. A variety of antibiotics were applied at both farms leading to antibiotics excretion of several hundred grams per farm per day. Sulfonamides, tetracyclines, and their epimers/isomers, and lincomycin were most frequently detected. Yet, despite decades of use, antibiotic occurrence appeared constrained to within farm boundaries. The most frequent antibiotic detections were associated with lagoons, hospital pens, and calf hutches. When detected below ground, tetracyclines were mainly found in soils, whereas sulfonamides were found in shallow groundwater reflecting key differences in their physicochemical properties. In manure lagoons, 10 compounds were detected including tetracyclines and trimethoprim. Of these 10, sulfadimethoxine, sulfamethazine, and lincomycin were found in shallow groundwater directly downgradient from the lagoons. Antibiotics were sporadically detected in field surface samples on fields with manure applications, but not in underlying sandy soils. Sulfadimethoxine and sulfamethazine were detected in shallow groundwater near field flood irrigation gates, but at highly attenuated levels.	Watanabe et al. 2010

TRFIA **Enivornmental water**	Using monoclonal antibodies labeled with EU3+ chelates, time-resolved fluoroimmunoassay (TRFIA) methods were developed for the determination of trace sulfamethazine (SMZ), sulfamethoxazole (SMX), and sulfadiazine (SDZ) in environmental waters. Under the optimized conditions, the developed methods offered (i) low detection limits (9.8 ng/l SMZ, 6.1 ng/l SMX, and 5.4 ng/l SDZ, based on 90% inhibition) which were about I order of magnitude lower than that of the enzyme-linked immunosorbent assay (ELISA), (ii) high selectivity with no cross-reactivity (< 0.05%) to similarly structured sulfonamides; (iii) high tolerance to variation of the sample pH (6.0–9.0) and salinity (0–100mM), as well as the presence of humic acid (0–100 mg/l DOC) and heavy metals (0–1 mg/l concentration each of Cu^{2+}, Cd^{2+}, Hg^{2+}, Pb^{2+}, and As(V)) in the samples, and (iv) direct determination with low cost high sample throughput, and low sample consumption (50–100 µl). The proposed TRFIA procedures were applied to determine sulfonamides in a variety of surface water and wastewater samples without sample pretreatment other than filtration. The satisfactory recoveries (64–127%) and reproducibilities (CV = 0.2–16%) achieved, as well as the good agreement with those given by liquid chromatography-tandem mass spectroscopy and ELISA methods, demonstrated the applicability of the proposed TRFIA methods for routine screening/quantification of sulfonamides in environmental waters.	Zhang et al. 2010
Livestock and poultry feedlots **Dung, manure**	The residue levels of selected fluoroquinolones, sulfonamides and tetracyclines in 143 animal dung samples collected in 2007 from large-scale livestock and poultry feedlots in 8 provinces were determined by using ultrasonic extraction and liquid chromatography. Recoveries from spiked pig dung samples (spike level = 1 mg/kg) ranged from 73.9 to 102.0% for fluoroquinolones, from 81.6 to 923% for sulfonamides. and from 57.2 to 72.6% for tetracyclines. Relative standard deviations of the recoveries were less than 10% within the same day. Method quantification limits were measured from 0.031 to 0.150 mg/kg for fluoroquinolones, from 0.023 to 0.082 mg/kg for sulfonamides, and 0.091 to 0.182 mg/kg for tetracyclines in spiked pig manure samples. Analysis of 61 pig, 54 chicken and 28 cow dung samples collected in China revealed that in pig and cow dung, up to 33.98 and 29.59 mg/kg ciprofloxacin, 33.26 and 46.70 mg/kg enrofloxacin, 59.06 and 59.59 mg/kg oxytetracycline, and 21.06 and 27.59 mg/kg chlortetracycline could be detected, respectively. A maximum concentration of 99.43 mg/kg fleroxacin, 225.45 mg/kg norfloxacin, 45.59 mg/kg ciprofloxacin and 1420.76 mg/kg enrofloxacin could be detected in chicken dung. No appreciable sulfonamide antibiotic concentrations (less than 10 mg/kg) were found in any animal dung, and only sulfadimidine was observed, at a maximum concentration of 6.04 mg/kg, in chicken dung. Both enrofloxacin and chlortetracycline were detected with a very high occurrence in three animal manure samples. The residue levels for most antibiotics showed significant statistical differences among the sampling districts and the animal species.	Zhao et al. 2010
Leaching **Lysimeter-based studies** **Transport to groundwater**	Antibiotics may be released to soils during the application of manure as fertiliser to land. The compounds may subsequently be transported to and contaminate groundwater and surface waters. This paper describes a series of lysimeter-based studies to explore the leaching behaviour of three veterinary antibiotics (sulfachloropyridazine, oxytetracycline and tylosin) under different conditions that could occur in the agricultural environment. The specific objectives were to: (1) explore the influence of slurry amendment and incorporation on leaching; (2) assess the effects of climate on leaching behaviour; and (3) evaluate the predictive capability of a leaching model used in the regulatory assessment of veterinary medicines. Sulfachloropyridazine was detected sporadically in leachate at concentrations up to 0.66 µg/l under typical irrigation conditions and more frequently at concentrations up to 8.5 µg/l under extreme irrigation conditions. incorporation and timing of rainfall had no effect on leaching behaviour. Oxytetracycline and tylosin were not detected in any leachate samples. These differences in behaviour were explained by the sorption and persistence characteristics of the compounds. Comparison of the experimental measurements with simulations from the leaching model indicated that the model greatly underestimates the transport of antibiotics to groundwater which raises questions over the application of these models in the regulatory risk assessment process.	Blackwell et al. 2009
Sulphonamides **Environmental hazards**	In recent years, concern regarding the environmental presence of sulfonamides (SAs) and other species of antibiotics has increased considerably due mainly to the potential spread of antimicrobial resistance in the different bacterial communities. However, many other ecotoxicological effects due to the release of these drugs in the different ecosystems may also be taking place. Analytical chemistry plays an important role in evaluating ecotoxicity through unequivocal identification and precise quantification of target compounds even when concentrations are very small. We aim to review all the studies carried out to date on potential environmental hazards posed by the SAs and to comment on the usefulness of chemical analysis in this application.	Garcia-Galan et al. 2009

Table 5. The risk posed by sulfonamides in soil and water

RISKS		
Biogas plant **Inhibition of aerobic fermentation**	Antibiotics of inorganic and organic origin in pig manure can inhibit the anaerobic process in biogas plants. The influence of three frequently used antibiotics, copper dosed as $CuSO_4$, sulfadiazine (SDZ), and difloxacin (DIF), on the anaerobic digestion process of pig manure was studied in semi-continuous experiments. ODM. Inhibitory effect of SDZ and DIF was observed at concentrations as high as 2.70 g/kg ODM and 0.54 g/kg ODM, respectively. It seems very unlikely that the antibiotics tested would inhibit the anaerobic process in a full-scale biogas plant.	Guo et al. 2012
Sulfamethoxazole **Electrochemical oxidation** **Degradation** **Toxicity of products**	Sulfamethoxazole (SMX) is a synthetic antibiotic widely applied as a bacteriostatic drug to treat a number of diseases. SMX can persist in the environment for long periods of time because of its low biodegradability, which may result in various, direct and indirect, toxicological effects on the environment and on human health. Therefore, we have developed the electrochemical advanced oxidation process (AOP) "electro-Fenton" to degrade SMX in aqueous media. In this work, a detailed study of the evolution of toxicity of SMX and its degradation products in aqueous solutions, during treatment by the electro-Fenton AOP, is described, using the bioluminescence MicrotoxA (R) method, based on the inhibition of luminescence of marine bacteria Vibrio fischeri. Samples were collected at various electrolysis times and analyzed by HPLC for quantifying the evolution of the degradation products, and their toxicity was measured by the MicrotoxA (R) method. Our results demonstrated that the toxicity of SMX aqueous solutions varied considerably with the electrolysis time and the applied current intensity. This phenomenon could be explained by the formation and disappearance of several degradation products, including cyclic and/or aromatic intermediates, and short-chain acid carboxylic acids, having a toxicity different of the initial antibiotic. The curves of the % of bacterial luminescence inhibition vs. electrolysis time, corresponding to the evolution of the toxicity of the formed degradation products, were investigated and tentatively interpreted.	Dirany et al. 2011
Ebro River basin water **Wastewater treatment plants** **Hazard quotients**	In the present work, the presence of 16 SAs and one of their acetylated metabolites in different water matrices of the Ebro River basin has been evaluated during two different sampling campaigns carried out in 2007 and 2008. Influent and effluent samples from seven wastewater treatment plants (WWTPs), together with a total of 28 river water samples were analyzed by on-line solid phase extraction-liquid chromathography-tandem mass spectrometry (on-line SPE-LC-MS/MS). Sulfamethoxazole and sulfapyridine were the SAs most frequently detected in WWTPs (96–100%), showing also the highest concentrations, ranging from 27.2 ng/l to 596 ng/l for sulfamethoxazole and from 3.7 ng/l to 227 ng/l for sulfapyridine. Sulfamethoxazole was also the SA most frequently detected in surface waters (85% of the samples) at concentrations between 11 ng/l and 112 ng/l. In order to assess the effectiveness of the wastewater treatment in degrading SAs, removal efficiencies in the seven WWTPs were calculated for each individual SA (ranging from 4% to 100%) and correlated to the corresponding hydraulic retention times or residence times of the SAs in the plants. SAs half-lives were also estimated, ranging from to 2.5 h (sulfadimethoxine) to 128 h (sulfamethazine). The contribution of the WWTPs to the presence of SAs depends on both the load of SAs discharging on the surface water from the WWTP effluent but also on the flow of the receiving waters in the discharge sites and the dilution exerted; WWTP4 exerts the highest pressure on the receiving water course. Finally, the potential environmental risk posed by SAs was evaluated calculating the hazard quotients (HQ) to different non-target organisms in effluent and river water. The degree of susceptibility resulted in algae > daphnia > fish. Sulfamethoxazole was the only SA posing a risk to algae in effluent water, with an HQ > 7.	Garcia-Galan et al. 2011b

Swine manure **Swine lagoon effluent** **Soil** **E. coli** **Antibiotic resistance genes**	The prevalence of ten antibiotic resistance genes (ARGs) was evaluated in a total of 616 Escherichia coli isolates from swine manure, swine lagoon effluent, and from soils that received lagoon effluent on a commercial swine farm site in Sampson County, North Carolina (USA). Isolates with ARGs coding for streptomycin/spectinomycin (aadA/strA and strB), tetracycline (tetA and tetB), and sulfonamide (sul1) occurred most frequently (60.6–91.3%). The occurrence of E. coli isolates that carried aadA, tetA, tetB, and tetC genes was significantly more frequent in soil samples (34.0–97.2%) than in isolates from lagoon samples (20.9–90.6%). Furthermore, the frequency of isolates that contain genes coding for aadA and tetB was significantly greater in soil samples (82.6–97.2%) when compared to swine manure (16.8–86.1%). Isolates from the lagoon that carried tetA, tetC, and sul3 genes were significantly more prevalent during spring (63.3–96.7%) than during winter (13.1–67.8%). The prevalence of isolates from the lagoon that possessed the strA, strB, and sul1 resistance genes was significantly more frequent during the summer (90.0–100%) than during spring (66.6–80.0%). The data suggest that conditions in the lagoon, soil, and manure may have an impact on the occurrence of E. coli isolates with specific ARGs. Seasonal variables seem to impact the recovery isolates with ARGs; however, ARG distribution may be associated with.	Graves et al. 2011
Liquid manure **Sulfadiazine in soil** **Microbial biomass**	Both manure and antibiotics affect the soil microbial community. We performed a microcosm experiment for up to 32 d to clarify whether the function and structure of the soil microbial community is differently affected by interactions of manure and the antibiotic sulfadiazine (SDZ). To this end selected concentrations of pig liquid manure (0, 20, 40, 80 g/kg) and SDZ (0, 10, 100 µg/kg) were combined. We hypothesized that incremental manure amendment might reduce the effect of SDZ in soils, due to an increasing sorption capacity of SDZ to organic compounds. Clear dose-dependent effects of SDZ on microbial biomass and PLFA pattern were determined, and SDZ effects interacted with the liquid manure application rate. Soil microbial biomass increased with incremental liquid manure addition, whereas this effect was absent in the presence of additional SDZ. However, activities of enzymes such as urease and protease were only slightly affected and basal respiration was not affected by SDZ application, while differences mostly depended on the concentration of liquid manure. These results illustrated that the microbial biomass and structural composition react more sensitive to SDZ contamination than functional processes. Furthermore, effects disproportionally increased with incremental liquid manure addition, although extractable amounts of SDZ declined with increasing liquid manure application.	Hammesfahr et al. 2011
Pig manure, soil **Sulfonamide resistance genes**	Two soils were amended three times with pig manure. The abundance of sulfonamide resistance genes was determined by quantitative PCR 2 months after each application. In both soils treated with sulfadiazine-containing manure, the numbers of copies of sul1 and sul2 significantly increased compared to numbers after treatments with antibiotic-free manure or a control and accumulated with repeated applications.	Heuer et al. 2011
Soil Phytotoxicity **Root elongation**	We applied a screening-level phytotoxicity assay to evaluate the effects of 10 antibiotics (at concentrations ranging from 1 to 10 000 µg/l) on germination and early plant growth using three plant species: lettuce (Lactuca sativa), alfalfa (Medicago sativa), and carrot (Daucus carota). The range of phytotoxicity of the antibiotics was large, with EC (25)s ranging from 3.9 µg/l to > 10,000 µg/l. Chlortetracycline, levofloxacin, and sulfamethoxazole were the most phytotoxic antibiotics. D. carota was the most sensitive plant species, often by an order of magnitude or more, followed by L. sativa and then M. sativa. Plant germination was insensitive to the antibiotics, with no significant decreases up to the highest treatment concentration of 10 000 µg/l. Compared with shoot and total length measurements, root elongation was consistently the most sensitive end point. Overall, there were few instances where measured soil concentrations, if available in the publicly accessible literature, would be expected to exceed the effect concentrations of the antibiotics evaluated in this study. The use of screening assays as part of a tiered approach for evaluating environmental impacts of antibiotics can provide insight into relative species sensitivity and serve as a basis by which to screen the potential for toxic effects of novel compounds to plants.	Hillis et al. 2011

RISK		
Liao River basin water **Liaodong Bay water** **Sulphonamides** **Source apportionment**	In the present study we investigated the occurrence of 19 sulfonamides, five N-acetylated sulfonamide metabolites, and trimethoprim in the Liao River basin and adjacent Liaodong Bay, China, as well as 10 human/agricultural source samples. Within the 35 river samples, 12 sulfonamides, four acetylated sulfonamides, and trimethoprim were detected, with the dominant being sulfamethoxazole (66.6 ng/l), N-acetylsulfamethoxazole (63.1 ng/l), trimethoprim (29.0 ng/l), sulfadiazine (14.0 ng/l), and sulfamonomethoxine (8.4 ng/l); within the 36 marine samples, 10 chemicals were detected, with the main contributions from sulfamethoxazole (25.2 ng/l) and N-acetylsulfamethoxazole (28.6 ng/l). Sulfamethoxazole (25.9%), N-acetylsulfamethoxazole (46.6%), trimethoprim (22.9%), and sulfapyridine (1.4%) were the main chemicals from human sources, while sulfamonomethoxine, sulfamethazine, sulfaquinoxaline, sulfaguanidine, sulfadiazine, sulfanilamide, and sulfamethoxypyridazine were dominant in the animal husbandry sources, specifically, swine and poultry farms, and sulfamethoxazole (91%) was dominant in the mariculture source. A principal component analysis with multiple linear regression was performed to evaluate the source apportionment of total sulfonamides in Liaodong Bay. It was found that animal husbandry contributed 15.2% of total sulfonamides, while human sources contributed 28.5%, and combined human and mariculture sources contributed 56.3%. In addition, the mariculture contribution was 24.1% of total sulfonamides into the sea based on mass flux estimation. The present study is the first report that the environmental levels of sulfonamide metabolites were comparable to the corresponding parents; therefore, we should pay attention to their environmental occurrence. Source apportionment showed human discharge (60.7%) significantly contributed to these antibiotics in Liaodong Bay, which provides important information for environmental management.	Jia et al. 2011
Huangpu River water **Sulphonamides** **Livestock role**	Water samples were collected from 19 sampling sites along the Huangpu River in June and December 2009. The occurrence, distribution and seasonal variation of 22 antibiotics, including four tetracyclines, three chloramphenicols, two macrolides, six fluoroquinolones, six sulfonamides and trimethoprim were investigated. It was found that all 19 sampling sites were contaminated by antibiotics. Four antibiotics (sulfamerazine, norfloxacin, fleroxacin and sarafloxacin) were not detected. The detection frequencies of the other 18 antibiotics were in the range of 5.3–100%. The median concentrations of the detected antibiotics ranged from quantification limits to 36.71 ng/l (tetracycline) in June and to 313.44 ng/l (sulfamethazine) in December. The number of detected antibiotics and the overall antibiotic concentrations were higher in December than in June due to the different river flow conditions. Different dominant antibiotics were observed for each group of antibiotics between June and December. Higher total concentrations of veterinary antibiotics such as tetracyclines were observed in suburban sampling sites than in unban sites, indicating the role of livestock and agricultural activities as an important source of antibiotic contamination.	Jiang et al. 2011
E. coli resistance	This study describes the genotypic characteristics of a collection of 100 multidrug-resistant (MDR) Escherichia coli strains recovered from cattle and the farm environment in Ireland in 2007. The most prevalent antimicrobial resistance identified was to streptomycin (100%), followed by tetracycline (99%), sulfonamides (98%), ampicillin (82%), and neomycin (62%). Resistance was mediated predominantly by strA-strB (92%), tetA (67%), sul2 (90%), bla (TEM) (79%), and aphA1 (63%) gene markers, respectively. Twenty-seven isolates harbored a class 1 integrase (intI1), while qacE Delta 1 and sul1 markers were identified in 25 and 26 isolates, respectively. The variable regions of these integrons contained aminoglycoside, trimethoprim, and beta-lactam resistance determinants (aadA12, aadB-aadA1, bla (OXA-30)-aadA1, dfrA1-aadA1, dfrA7). Class 2 integrons were identified less frequently (4%) and contained the gene cassette array dfrA1-sat1-aadA1. Resistance to ampicillin, neomycin, streptomycin, sulfonamide, and tetracycline was associated with transferable high-molecular-weight plasmids, as demonstrated by conjugation assays. A panel of virulence markers was screened for by PCR, and genes identified included vt1, K5 in two isolates, papC in 10 isolates, and PAI IV (536) in 37 isolates. MDR commensal E. coli isolates from Irish cattle displayed considerable diversity with respect to the genes identified. Our findings highlight the importance of the commensal microflora of food-producing animals as a reservoir of transferable MDR.	Karczmarczyk et al. 2011

E. coli resistance roilers **Management factors**	A cross-sectional study on 32 different Belgian broiler farms was performed in 2007 and 2008 to identify risk factors for ceftiofur resistance in Escherichia coli. On each farm, one E. coli colony was isolated from 30 random birds. Following susceptibility testing of 14 antimicrobials, an on-farm questionnaire was used to obtain information on risk factors. Using a multilevel logistic regression model two factors were identified at the animal level : resistance to amoxicillin and to trimethoprim-sulfonamide. On the farm level, besides antimicrobial use, seven management factors were found to be associated with the occurrence of ceftiofur resistance in E. coli from broilers : poor hygienic condition of the medicinal treatment reservoir, no acidification of drinking water, more than three feed changes during the production cycle, hatchery of origin, breed, litter material used, and treatment with amoxicillin. This study confirms that not only on-farm antimicrobial therapy, but also management-and hatchery-related factors influence the occurrence of antimicrobial resistance.	Persoons et al. 2011
Pig manure **Bacterial resistance**	This study aimed to investigate the association between antibiotic residues and bacterial antimicrobial resistance in liquid pig manure used as fertilizer. Concentrations of tetracyclines (TETs) and sulfonamides (SULs) were determined by liquid chromatography-mass spectrometry in 305 pig manure samples; antibiotic contents were correlated to the phenotypic resistance of Escherichia coli ($n = 613$) and enterococci ($n = 564$) towards up to 24 antibiotics. In 121 samples, the concentration of the TET resistance genes tet(M), tet(O) and tet(B) was quantified by real-time-PCR. TETs were found in 54% of the samples. The median sum concentration of all investigated TETs in the positive samples was 0 center dot 73 mg/kg. SULs were found with a similar frequency (51%) and a median sum concentration of 0 center dot 15 mg/kg in the positive samples. Associated with the detection of TETs and/or SULs, resistance rates were significantly elevated for several substances – some of them not used in farm animals, e.g. chloramphenicol and synercid. In addition, multiresistant isolates were found more often in samples containing antibiotics. Analysis of the resistance genes tet(M) and tet(O) already showed a significant increase in their concentrations – but not in tet(B) – in the lowest range of total TET concentration. Mean tet(M) concentrations increased by the factor of 4 center dot 5 in the TET concentration range of 0 center dot 0.1–1 mg/kg, compared to negative manure samples. Antibiotic contamination of manure seems to be associated with a variety of changes in bacterial resistance, calling for a prudent use of antibiotics in farm animals.	Holzel et al. 2010
Sulfonamide resistance genes **Manured soil Pig slurry**	The prevalences of three sulfonamide resistance genes, sul1, sul2, and sul3 and sulfachloropyridazine (SCP) resistance were determined in bacteria isolated from manured agricultural clay soils and slurry samples in the United Kingdom over a 2-year period. Slurry from tylosin-fed pigs amended with SCP and oxytetracycline was used for manuring. Isolates positive for sul genes were further screened for the presence of class 1 and 2 integrons. Phenotypic resistance to SCP was significantly higher in isolates from pig slurry and postapplication soil than in those from preapplication soil. Of 531 isolates, 23% carried sul1, 18% sul2, and 9% sul3 only. Two percent of isolates contained all three sul genes. Class 1 and class 2 integrons were identified in 5% and 11.7%, respectively, of sul-positive isolates. In previous reports, sul1 was linked to class 1 integrons, but in this study only 8% of sul1-positive isolates carried the intI1 gene. Sulfonamide-resistant pathogens, including Shigella flexneri, Aerococcus spp., and Acinetobacter baumannii, were identified in slurry-amended soil and soil leachate, suggesting a potential environmental reservoir. Sulfonamide resistance in Psychrobacter, Enterococcus, and Bacillus spp. is reported for the first time, and this study also provides the first description of the genotypes sul1, sul2, and sul3 outside the Enterobacteriaceae and in the soil environment.	Byrne-Bailey et al. 2009

RISK		
Antibiotic resistance genes **Self-transferable replicons** **Plasmids**	Bioactive amounts of antibiotics as well as resistant bacteria reach the soil through manure fertilization. We investigated plasmids that may stimulate the environmental spread and interspecies transfer of antibiotic resistance. After treatment of two soils with manure, either with or without the sulfonamide antibiotic sulfadiazine, a significant increase in copies of the sulfonamide resistance gene sul2 was detected by qPCR. All sul2 carrying plasmids, captured in Escherichia coli from soil, belonged to a novel class of self-transferable replicons. Manuring and sulfadiazine significantly increased the abundance of this replicon type in a chemically fertilized but not in an annually manured soil, as determined by qPCR targeting a transfer gene. Restriction patterns and antibiograms showed a considerable diversity within this novel plasmid group. Analysis of three complete plasmid sequences revealed a conserved 30 kbp backbone with only 36% G + C content, comprised of transfer and maintenance genes with moderate homology to plasmid pIPO2 and a replication module (rep and oriV) of other descent. The plasmids differed in composition of the 27.0–28.3 kbp accessory region, each of which carried ISCR2 and several resistance genes. Acinetobacter spp. was identified as a potential host of such LowGC-type plasmids in manure and soil.	Heuer et al. 2009
Manure **Soil** **Plant growth** **cotoxicology**	The potential impact of six antibiotics (chlortetracycline, tetracycline and tylosin; sulfamethoxazole, sulfamethazine and trimethoprim) on plant growth and soil quality was studied by using seed germination test on filter paper and plant growth test in soil, soil respiration and phosphatase activity tests. The phytotoxic effects varied between the antibiotics and between plant species (sweet oat, rice and cucumber). Rice was most sensitive to sulfamethoxazole with the EC10 value of 0.1 mg/l. The antibiotics tested inhibited soil phosphatase activity during the 22 days' incubation. Significant effects on soil respiration were found for the two sulfonamides (sulfamethoxazole and sulfamethazine) and trimethoprim, whereas little effects were observed for the two tetracyclines and tylosin. The effective concentrations (EC10 values) for soil respiration in the first two days were 7 mg/kg for sulfamethoxazole, 13 mg/kg for sulfamethazine and 20 mg/kg for trimethoprim. Antibiotic residues in manure and soils may affect soil microbial and enzyme activities. Terrestrial ecotoxicological effects of antibiotics are related to their sorption and degradation behavior in soil.	Liu et al. 2009
Inhibition of soil microbial functions **Resistance genes**	Sulfonamides can inhibit soil microbial functions and enhance the spread of resistance genes among soil microorganisms. in order to assess the exposure of soil microorganisms to SDZ, a conceptual kinetic model for the prediction of temporally resolved antibiotic concentrations in soil was developed. The model includes transformation reactions. reversible sequestration and the formation of non-extractable residues (NER) from SDZ and its main metabolites N-4-acetyl-sulfadiazine (N-ac-SDZ) and 4-hydroxy-sulfadiazine (OH-SDZ). The optimum model structure and rate constants of SDZ kinetics and its metabolites were determined by fitting different model alternatives to sequential extraction data of a manure-amended Cambisol soil. N-ac-SDZ is degraded to SDZ with a half-life of four day, whereas OH-SDZ is not. Though, based on the available data, the hydroxylation of SDZ seems to be negligible, it is still included in the model structure since this process has been observed in recent studies. Sequestration into a residual fraction has similar kinetics for SDZ, N-ac-SDZ and OH-SDZ and is one order of magnitude faster than the reverse translocation. The irreversible formation of NER is restricted to SDZ and OH-SDZ. The model shows good agreement when applied to extraction data measured independently for a Luvisol soil. The combination of sequential extraction data and the conceptual kinetic model enables us to gain further insight into the long-term fate and exposure of sulfonamides in soil.	Zarfl et al. 2009

Table 6. Movement and transformation of sulfonamides in manure, soil and water

TRANSFORMATION		
Pollutants degradation **Ferrate(VI) technology**	Nitrogen-containing pollutants have been found in surface waters and industrial wastewaters due to their presence in pesticides, dyes, proteins, and humic substances. Treatment of these compounds by conventional oxidants produces disinfection by-products (DBP). Ferrate(VI) ($Fe^{VI}O_4^{2-}$, Fe(VI)) is a strong oxidizing agent and produces a non-toxic by-product Fe(III), which acts as a coagulant. Ferrate(VI) is also an efficient disinfectant and can inactivate chlorine resistant microorganisms. A novel ferrate(VI) technology can thus treat a wide range of pollutants and microorganisms in water and wastewater. The aim of this paper is to review the kinetics and products of the oxidation of nitrogen-containing inorganic (ammonia, hydroxylamine, hydrazine, and azide) and organic (amines, amino acids, anilines, sulfonamides, macrolides, and dyes) compounds by ferrate(VI) in order to demonstrate the feasibility of ferrate(VI) treatment of polluted waters of various origins. Several of the compounds can degraded in seconds to minutes by ferrate(VI) with the formation of non-hazardous products. The mechanism of oxidation involves either one-electron or two-electrons processes to yield oxidation products. Future research directions critical for the implementation of the ferrate(VI)-based technology for wastewater and industrial effluents treatment are recommended.	Sharma 2010
Concentration during composting	The purpose of this study was to understand the influence of the composting process and the components of the compost on the levels of three common classes of antibiotics (tetracyclines, sulfonamides, and macrolides). Composted materials at different stages of composting were collected from compost manufacturing plants and the variation in antibiotic concentrations was determined. Three different antibiotics, chlortetracycline (CTC), sulfamethazine (SMZ), and tylosin (TYL) at three different concentrations (2, 10, and 20 µg/kg) were also applied to a mixture of pig manure and sawdust and the mixtures incubated using a laboratory scale composting apparatus to monitor the changes in antibiotic concentrations during composting together with the physicochemical properties of the composts. During composting, in both field and lab-scale investigations, the concentrations of all three different antibiotics declined below the relevant Korean guideline values (0.8 µg/kg for tetracyclines, 0.2 µg/kg for sulfonamides and 1.0 µg/kg for macrolides). The decline of tetracycline and sulfonamide concentrations was highly dependent on the presence of sawdust while there was no influence of sawdust on TYL decline.	Kim et al. 2012
Transport in saturated porous media **Laboratory experiments** **Mathematical model**	Many antibiotics regarded as emerging contaminants have been frequently detected in soils and groundwater; however, their transport behaviours in soils remain largely unknown. This study examined the transport of two antibiotics, sulfamethoxazole (SMZ) and ciprofloxacin (CIP), in saturated porous media. Laboratory columns packed with quartz sand was used to test the effects of solution pH and ionic strength (IS) on their retention and transport. The results showed that these two antibiotics behaved differently in the saturated sand columns. In general, SMZ manifested a much higher mobility than CIP for all experimental conditions tested. Almost all SMZ transported through the columns within one pore volume in deionized water (i.e., pH = 5.6, IS = 0), but no CIP was detected in the effluents under the same condition after extended column flushing. Perturbations in solution pH (5.6 and 9.5) and IS (0 and 0.1M) showed no effect on SMZ transport in the saturated columns. When pH increased to 9.5, however, similar to 93% of CIP was eluted from the sand columns. Increase of IS from 0 to 0.1M also slightly changed the distribution of adsorbed CIP within the sand column at pH 5.6, but still no CIP was detected in the effluents. A mathematical model based on advection-dispersion equation coupled with equilibrium and kinetic reactions successfully simulated the transport of the antibiotics in water-saturated porous media with $R^2 = 0.99$.	Chen et al. 2011

TRANSFORMATION		
Sewage sludge **Sulfamethazine degradation** **White-rot fungus** **Trametes versicolor**	Degradation of the sulfonamide sulfamethazine (SMZ) by the white-rot fungus Trametes versicolor was assessed. Elimination was achieved to nearly undetectable levels after 20 h in liquid medium when SMZ was added at 9 mg/l. Experiments with purified laccase and laccase-mediators resulted in almost complete removal. On the other hand, inhibition of SMZ degradation was observed when piperonilbutoxide, a cytochrome P450-inhibitor, was added to the fungal cultures. UPLC-QqTOF-MS analysis allowed the identification and confirmation of 4 different SMZ degradation intermediates produced by fungal cultures or purified laccase: desulfo-SMZ, N_4-formyl-SMZ, N_4-hydroxy-SMZ and desamino-SMZ; nonetheless SMZ mineralization was not demonstrated with the isotopically labeled sulfamethazine-phenyl-$^{13}C_6$ after seven days. Inoculation of T. versicolor to sterilized sewage sludge in solid-phase systems showed complete elimination of SMZ and also of other sulfonamides (sulfapyridine, sulfathiazole) at real environmental concentrations, making this fungus an interesting candidate for further remediation research.	Garcia-Galan et al. 2011a
Groundwater **Nitrogen-limiting biobarrier** **Slow-sand-filter** **Sulfachloropyridazine (SCP) removal**	Two types of microbial reactors were evaluated as methods for removing SCP from flowing water. One type of reactor evaluated was a nitrogen-limiting biobarrier; the other a slow-sand-filter. Results showed that the soybean oil-fed, nitrogen-limiting biobarrier was not very effective at removing SCP from flowing water. When supplied with flowing water containing 2.4 mg/l SCP the nitrogen-limiting biobarrier removed similar to 0.6 mg/l SCP or about 28% of that present. SCP removal by the nitrogen-limiting biobarrier may not have been biological as abiotic removal was not ruled out. More efficient biological removal was obtained with the slow-sand-filter which reduced the SCP levels from 2.35 to 0.048 mg/l, a removal efficiency of similar to 98%. High levels of nitrate nitrogen, 50 mg/l N, did not interfere with the removal processes of either reactor suggesting that SCP was not being degraded as a microbial nitrogen source.	Hunter and Shaner 2011
Marine shrimp pond **Water and sediment** **Natural light** **Microbial activities**	Water and sediment collected from a marine shrimp pond were examined and a factorial design was employed to evaluate the effects of selected parameters. The results showed that all the SAs in water and sediment had significant declines attributed to natural light and microbial activities. The half-lives (t (1/2 s)) of SAs in non-sterile water and sediment samples under natural light were 2.0–15.0 and 0.7–7.3 days, respectively, and slowed to 2.9–62.9 and 6.9–85.6 days after sterilized. Moreover, the declines of SAs were significantly faster under ultraviolet than visible light: with 36.5–70.9% shorter t (1/2) s. Anaerobic condition was also effective on declines of SAs in sediment. Both sulfate-reducing and methanogenic microbes were directly involved in the decline of SDM, and indirectly contributed to SMX declines.	Lai et al. 2011
Wastewater treatment plants **Sulfamethoxazole** **Bacterial degradation**	Sulfamethoxazole (SMX) removal in conventional wastewater treatment plants (WWTPs) ranges from 0% to 90%, and there are opposing results regarding its biodegradability at lab scale. The objective of this research was to determine the ability of pure cultures of individual and mixed consortia of bacteria (Bacillus subtilis, Pseudomonas aeruginosa, Pseudomonas putida, Rhodococcus equi, Rhodococcus erythropolis, Rhodococcus rhodocrous, and Rhodococcus zopfii) known to exist in WWTP activated sludge to remove SMX. Results showed that R. equi alone had the greatest ability to remove SMX leading to 29% removal (with glucose) and the formation of a metabolite. Degradation pathways and metabolite structures have been proposed based on the potential enzymes produced by R. equi. When R. equi was mixed with other microorganisms, a positive synergistic effect was not observed and the maximum SMX removal achieved was 5%. This indicates that pure culture results cannot be extrapolated to mixed culture conditions, and the methodology developed here to study the biodegradability of compounds under controlled mixed culture conditions offers an alternative to conventional studies using pure bacterial cultures or inocula from activated sludge sources consisting of unknown and variable microbial populations.	Larcher and Yargeau 2011

Swine wastewater **Sulfonamide removal** **UV irradiation**	The large-scale application of veterinary antibiotics in livestock industry makes swine wastewater an important source of antibiotic pollution. The effective removal of antibiotics in swine wastewater seems necessary. UV irradiation was employed for removal of five selected veterinary antibiotics, sulfamethoxazole (SMX), sulfathiazole (STZ), sulfamethazine (SMN), sulfamethizole (SML) and sulfadimethoxine (SDM), which are commonly found in swine wastewater. The effect of initial pH and reaction time on antibiotic removal was examined, and the reaction kinetics were studied. Both pH value and reaction time for the removal were optimized to be 7.0 and 60 min, respectively. Under the optimized conditions, the five selected antibiotics were effectively removed with removal efficiency of .00%, 98.7%, 96.3%, 99.0% and 100% for SMX, STZ, SMN, SML and SDM, respectively. The degradation reaction was found to fit the first-order kinetic well. Veterinary antibiotics SMX, STZ, SMN, SML and SDM can be effectively removed under UV irradiation, and pH value as well. is reaction time have obvious effects on the degradation. The reaction mechanism was suggested to be mainly the direct photo-degradation.	Li et al. 2011a
Wastewater sludge **Antibiotic resistance genes** **Thermal digestiol** **Bacterial community**	Wastewater treatment processes are of growing interest as a potential means to limit the dissemination of antibiotic resistance. This study examines the response of nine representative antibiotic resistance genes (ARGs) encoding resistance to sulfonamide (sulI, sulII), erythromycin (erm(B), erm(F)), and tetracycline (tet(O), tet(W), tet(C), tet(G), tet(X)) to various laboratory-scale sludge digestion processes. The class I integron gene (intI1) was also monitored as an indicator of horizontal gene transfer potential and multiple antibiotic resistance. Mesophilic anaerobic digestion at both 10 and 20 day solids retention times (SRTs) significantly reduced sulI, sulI, tet(C), tet(G), and tet(X) with longer SRT exhibiting a greater extent of removal; however, tet(W), erm(B) and erm(F) genes increased relative to the feed. Thermophilic anaerobic digesters operating at 47 degrees C, 52 degrees C, and 59 degrees C performed similarly to each other and provided more effective reduction of erm(B), erm(F), tet(0), and tet(W) compared to mesophilic digestion. However, thermophilic digestion resulted in similar or poorer removal of all other ARGs and intI1. Thermal hydrolysis pretreatment drastically reduced all ARGs, but they generally rebounded during subsequent anaerobic and aerobic digestion treatments. To gain insight into potential mechanisms driving ARG behavior in the digesters, the dominant bacterial communities were compared by denaturing gradient gel electrophoresis. The overall results suggest that bacterial community composition of the sludge digestion process, as controlled by the physical operating characteristics, drives the distribution of ARGs present in the produced biosolids, more so than the influent ARC composition.	Ma et al. 2011
Soil-water systems **Sorption** **Transport** **Degradation**	Sulfonamides (SAs) are one of the broadly used antibiotics in domestic animal operations and have a notable potential of entering the environment through animal manure management practices. In this study, sulfamethazine (SMZ) was used as a prototype to study the sorption, fate, and transport of SAs in soil-water systems using batch and miscible-displacement experiments. Sulfamethazine was degraded to a polar metabolite (PM). The batch experiments indicated that the linear sorption partitioning coefficient (Kd) values for the PM ranged from 7.5 to 206.2 l/kg. Strong relationships between the sorption of PM and various soil fractions and organic matter were also observed. The miscible-displacement experiments showed that 33–70% of SMZ was degraded within 6 h during transport in the soil columns. Also, 69–99.7% of SMZ and PM were recovered in the effluents suggesting their high mobility. Also, the simultaneous degradation, sorption, and transport of SMZ and PM were described using a two-site chemical nonequilibrium fate and transport model, using the Kd values obtained from the batch experiments. The parameters of this model were uniquely estimated using a global optimization strategy, the stochastic ranking evolutionary strategy.	Fan et al. 2011

TRANSFORMATION		
Hospital water effluent **Electrocoagulation** **Sulfonamides degradation**	In this study, an investigation was carried out into the occurrence of sulfamethoxazole (SMX) and trimethoprim (TMP) in the effluent of the university hospital (HUSM) of the UFSM. The degradation of these antimicrobials by the electrocoagulation (EC) process was also examined, in both the aqueous solution and hospital effluent, and a study was conducted in order to identify the subproducts formed. The experiments were optimized through factorial planning and, also, checked by response surface methodology. The best conditions for EC (achieving 58.0% of chemical oxygen demand (COD) reduction) were obtained by using 13 mA cm^2, 500 mg/l of NaCl, and 30 mm of interelectrode distance. The quantification of SMX (27.8 µg/l) and TMP (6.65 µg/l) in the hospital effluent, and the identification of the degradation products were carried out through liquid chromatography-mass spectrometry quadrupole linear and ion trapping with electrospray ionization (LC-ESI-MS/MS_QTrap). Removals of 88.0% (degradation only) and 33.0% (adsorption only) were achieved for aqueous solutions of SMX and TMP, respectively, under otimized conditions. In hospital effluent samples, fortified with additions of SMX and TMP, corresponding removals of 16.0% (degradation) and 28.0% (adsorption) were achieved. This suggests that the EC process is efficient in degrading SMX in aqueous solution, although the same was not the case with TMP. The degradation products of SMX were identified (m/z 256.0 and 288.5); however, only the latter is mentioned in the literature.	Martins et al. 2011
Soil **Sulfamethoxazole** **Fe(III)-reducing** **Sulfate-reducing**	Dissipation of the sulfonamide antimicrobial sulfamethoxazole was examined in soil microcosms incubated under different terminal electron-accepting conditions (aerobic, nitrate-reducing, Fe(III)-reducing, and sulfate-reducing). Somewhat unexpectedly, sulfamethoxazole dissipation was fastest under Fe(III)-reducing conditions, with concentrations decreasing by > 95% within 1 day. The rapid transformation was attributed to abiotic reactions between sulfamethoxazole and Fe(II) generated by microbial reduction of Fe(III) soil minerals. Separate experiments demonstrated that sulfamethoxazole was abiotically transformed in Fe(II)-amended aqueous suspensions of goethite (alpha-FeOOH$_{(s)}$), and observed rate constants varied with the extent of Fe(II) sorption to goethite. Sulfamethoxazole transformation is initiated by a 1-electron reductive cleavage of the N-O bond in the isoxazole ring substituent, and observed products are consistent with Fe(II)-mediated reduction and isomerization processes. These findings reveal potentially important, but previously unrecognized, pathways that may contribute to the fate of sulfamethoxazole and related chemicals in reducing soil environments.	Mohatt et al. 2011
Sewage treatment plants **Sulphonamides** **Poultry manure** **Swine manure**	In recent years, sludge generated in sewage treatment plants (STPs) and solid waste from livestock being utilized is useful for circulation of nourishment in farmlands as recycled organic manure (ROM). In this study, we determined the residue levels and patterns of 12 pharmaceutical products generated by human activity in the ROMs produced from human waste sludge (HWS), sewage sludge (SS), cattle manure (CM), poultry manure (PM), swine manure (SM) and horse manure (HM). The kind and number of pharmaceutical products detected in ROMs were different. Fluoroquinolones (FQs) were detected at high levels in HWS and SS samples. In addition, the detection frequency and concentration levels of sulfonamides (SAs) in PM and SM were high. Moreover, high concentrations of chlortetracycline (CTC) were found in only SM. These differences reflect specific adherence adsorption of the pharmaceutical products to different livestock and humans. Moreover, it was found that the concentrations of pharmaceutical products and fermentation levels of ROMs had significant positive correlation (r = 0.41, P = 0.024). When the fermentation test of ROM was conducted in a rotary fermentor in a lab scale test, the residue levels of pharmaceutical products decreased effectively except carbamazepine (CBZ). The rates of decrease were in the case of tetracyclines (TCs): 85–92%, FQs: 81–100%, erythromycine: 67%, SAs: 79–95%, trimethoprim: 86% and CBZ: 37% by 30 d. Pharmaceutical products that can be decomposed by fermentation process at the lowest impact of residual antibiotic activities may therefore be considered as environmentally friendly medicines.	Motoyama et al. 2011

Activated sludge **Membrane bioreactor** **Ultrafiltration** **Sulfamethoxazole**	The potential of membrane bioreactor (MBR) systems to remove organic micropollutants was investigated at different scales, operational conditions, and locations. The effluent quality of the MBR system was compared with that of a plant combining conventional activated sludge (CAS) followed by ultrafiltration (UF). The MBR and CAS-UF systems were operated and tested in parallel. An MBR pilot plant in Israel was operated for over a year at a mixed liquor suspended solids (MLSS) range of 2.8–10.6 g/l. The MBR achieved removal rates comparable to those of a CAS-UF plant at the Tel-Aviv wastewater treatment plant (WWTP) for macrolide antibiotics such as roxythromycin, clarithromycin, and erythromycin and slightly higher removal rates than the CAS-UF for sulfonamides. A laboratory scale MBR unit in Berlin – at an MLSS of 6–9 g/l – showed better removal rates for macrolide antibiotics, trimethoprim, and 5-tolyitriazole compared to the CAS process of the Ruhleben sewage treatment plant (STP) in Berlin when both were fed with identical quality raw wastewater. The Berlin CAS exhibited significantly better benzotriazole removal and slightly better sulfamethoxazole and 4-tolyltriazole removal than its MBR counterpart. Pilot MBR tests (MLSS of 12 g/l) in Aachen, Germany, showed that operating flux significantly affected the resulting membrane fouling rate, but the removal rates of dissolved organic matter and of bisphenol A were not affected.	Sahar et al. 2011
Sandy-textured soils **Sulphonamides** **Durable contamination** **Risks for groundwater contamination**	Spreading of urban wastewater on agricultural land may lead to concomitant input of organic and inorganic pollutants. Such multiple pollution sites offer unique opportunities to study the fate of both heavy metals and pharmaceuticals. We examined the occurrence and fate of selected antibiotics in sandy-textured soils, sampled four years after cessation of 100 years irrigation with urban wastewater from the Paris agglomeration. Previous studies on heavy metal contamination of these soils guided our sampling strategy. Six antibiotics were studied, including quinolones, with a strong affinity for organic and mineral soil components, and sulfonamides, a group of more mobile molecules. Bulk samples were collected from surface horizons in different irrigation fields, but also in subsurface horizons in two selected profiles. In surface horizons, three quinolones (oxolinic acid, nalidixic acid, and flumequine) were present in eight samples out of nine. Their contents varied spatially, but were well-correlated one to another. Their distributions showed great similarities regarding spatial distribution of total organic carbon and heavy metal contents, consistent with a common origin by wastewater irrigation. Highest concentrations were observed for sampling sites close to irrigation water outlets, reaching 22 µg/kg for nalidixic acid. Within soil profiles, the two antibiotic groups demonstrated an opposite behavior: quinolones, found only in surface horizons; sulfamethoxazole, detected in clay-rich subsurface horizons, concomitant with Zn accumulation. Such distribution patterns are consistent with chemical adsorption properties of the two antibiotic groups: immobilization of quinolones in the surface horizons ascribed to strong affinity for organic matter (OM), migration of sulfamethoxazole due to a lower affinity for OM and its interception and retention in electronegative charged clay-rich horizons. Our work suggests that antibiotics may represent a durable contamination of soils, and risks for groundwater contamination, depending on the physicochemical characteristics both of the organic molecules and of soil constituents.	Tamtam et al. 2011
Reference manure **Laboratory testing**	Veterinary medicines and biocides are frequently applied in animal houses of livestock husbandry. So far these substances are not transformed during manure storage, they enter soil by the application of manure as organic fertilizer. Therefore, biodegradability of veterinary medicines and biocides in manure is in the focus of regulatory procedures of environmental risk assessment. Since the representative and reproducible sampling of manures from high volume tanks is considered impossible due to high matrix variabilities, the reference manure concept was developed to utilize liquid bovine and pig manures for reproducible laboratory testing. Accordingly, excrement samples of cattle and pigs individually kept at experimental and conventional animal houses were taken. Tap water was added to matrix characterized excrements in order to prepare bovine and pig reference manures of 10 and 5% dry substance contents, respectively. Subsequently, the long-term transformation of selected C-14-labeled test substances was investigated under strictly anaerobic conditions. The application of different batches of bovine or pig reference manures indicated that extrapolation of transformation rates within the same animal species was possible. However, results cannot be transferred from bovine to pig manure because of substance specific interactions with the different manure matrices. The dependency of metabolic dynamics on different dry substance contents (2.5, 5, 10%) was additionally investigated in both manure matrices. These tests clearly showed that the dry substance content of the reference manure is one of the most relevant factors affecting the transformation of veterinary medicines and biocides. In contrast to highly variable tank manures, the reference manure concept allows for the exact adjustment of this parameter to guarantee reproducible laboratory testing.	Kreuzig 2010

Table 7. The most frequently used methods for sulfonamide detection

ANALYSIS		
Capillary electrophoresis	CE is popular due to its simplicity, speed, highly efficient separations and minimal solvent and reagent consumption; it can also be included as a useful technique in the nanotechnology field and it covers a wide range of specific applications in different fields (chemical, pharmaceutical, genetic, clinical, food and environmental). CE has been very well evaluated in research laboratories for several years, and different new approaches to improve sensitivity (one of the main drawbacks of CE) and robustness have been proposed. However, this technique is still not well accepted in routine laboratories for food analysis. Summarizing, the majority of CE scientific papers focus primarily on the effects upon the separation of the analytes while ignoring their behavior if these analytes are presented in real samples.	Pinero et al. 2011
Extraction **Sample preparation**	Monolith was first used as a material for chromatographic separation two decades ago and solid-phase extraction over 10 years, and since then, separation science has undergone a dramatic change owing to advancements in analytical technology. Recently, monolith has been modified to suit various devices for the extraction and enrichment of analytes in any matrices of environmental, food, and biological analyses. This approach has contributed to miniaturization and automation for sample preparation, and it can reduce the time and cost requirements of sample preparation.	Namera et al. 2011
Sample preparation	Monolithic columns with a unique structure possess some exceptional characteristics, which make them an excellent tool in the hands of analytical chemists, not only for separation but also for sample preparation. Their much higher external porosity compared to conventional particle-packed columns results in higher permeability and low-pressure drop with higher separation efficiency. Till now, monolithic columns have been applied to the analysis of different analytical matrices: pharmaceuticals, biofluids, food matrices, environmental samples, biochemical species, proteomics, etc.	Samanidou and Karageorgou 2011
HPLC **Pharmaceutical preparations** **Biological fluids**	HPLC can provide a valuable tool for generating highly pure preparations for characterizing the antimicrobial activities. In the present review article, column and mobile phase conditions as well as sample preparation issues are taken into consideration. A brief discussion on chemical structure, spectrum of activity and action mechanism of sulfonamides has also been provided. The time frame of papers covered by this review article starts at 1974 and ends at 2009.	Tolika et al. 2010
Capillary electrophoresis **Foodstuffs of animal origin** **Environmental samples**	In this paper we review applications of capillary electrophoresis (CE) to the determination of antibiotic residues in food derived from animals and in environmental samples. Due to the maximum residue limits established by the EU, in Directive 2377/90/EEC, for foodstuffs of animal origin and considering the low levels that can be found in environmental or waste waters or soils, different strategies to increase sensitivity have been developed, including off-line preconcentration, on-line stacking modes to use higher sample volumes, or in-line solid-phase extraction. Also, several detection techniques, such as fluorescence, laser-induced fluorescence, electrochemical detection, or mass spectrometry have been used; the last of these also enables unequivocal identification of the residues, required by Commission Decision 2002/657/EC.	Garcia-Campana et al. 2009
Immunochemical methods	ELISA methods; biosensors; fluorescence polarization immunoassay; and new promising methods for the detection of sulfamide drugs, immunochromatographic test strips, the method using molecularly imprinted polymers, piezoelectric quartz immunosensors, etc.	Nesterenko et al. 2009
HPLC-MS/MS **UV and fluorescence detection**	An over-view of analytical methodologies for the determination of quinolone (Qs) and fluoroquinolone (FQs), macrolide (MLs). tetracycline (TCs), sulfonamide (SAs) antibiotics and trimethoprim (TMP) in different environmental waters. The analysis of these antibiotics has usually been carried out by high-performance liquid chromatography (HPLC) coupled to mass spectrometry (MS) or tandem mass spectrometry (MS/MS) and to a lesser extent by ultraviolet (UV) or fluorescence detection (FD). A very important step before LC analysis is sample preparation and extraction leading to elimination of interferences and prevention of matrix effect and preconcentration of target analytes.	Seifrtova et al. 2009

Aquaculture water **Fast response sensor** **Flow-injection** **Potenciometric design**	Sulfadiazine is an antibiotic of the sulfonamide group and is used as a veterinary drug in fish farming. Monitoring it in the tanks is fundamental to control the applied doses and avoid environmental dissemination. Pursuing this goal, we included a novel potentiometric design in a flow-injection assembly. The electrode body was a stainless steel needle veterinary syringe of 0.8-mm inner diameter. A selective membrane of PVC acted as a sensory surface. Its composition, the length of the electrode, and other flow variables were optimized. The best performance was obtained for sensors of 1.5-cm length and a membrane composition of 33% PVC, 66% o-nitrophenyloctyl ether, 1% ion exchanger, and a small amount of a cationic additive. It exhibited Nernstian slopes of 61.0 mV per decade down to 1.0×10^{-5} mol/l, with a limit of detection of 3.1×10^{-6} mol/l in flowing media. All necessary pH/ionic strength adjustments were performed online by merging the sample plug with a buffer carrier of 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid, pH 4.9. The sensor exhibited the advantages of a fast response time (less than 15 s), long operational lifetime (60 days), and good selectivity for chloride, nitrite, acetate, tartrate, citrate, and ascorbate. The flow setup was successfully applied to the analysis of aquaculture waters. The analytical results were validated against those obtained with liquid chromatography-tandem mass spectrometry procedures. The sampling rate was about 84 samples per hour and recoveries ranged from 95.9 to 106.9%.	Almeida et al. 2011a, b
Sea water **Solid phase extraction** **LC-UV detection** **Sample preparation**	A new analytical method based on offline solid phase extraction and liquid chromatography with standard UV detection (SPE-FIPLC-UV) was developed to determine the presence of sulfonamides in seawaters. Special attention was paid to the sample preparation step. Different variables affecting the extraction process, such as seawater salinity and the humic acid content were studied. As a result, the presented SPE procedure for the extraction of sulfonamides from seawaters is also applicable to other techniques like LC-MS and LC-MS/MS. This method was optimized and fully validated for its performance parameters. It has very good selectivity, linearity ($R^2 > 0.995$), precision (RSD < 5%), accuracy (76.7–115.4%), as well as low limits of detection (LOD, 167 ng/l) and quantification (LOQ, 500 ng/l). This SPE procedure proved to be very effective (absolute recovery > 75%), even in highly saline waters and in the presence of humic acids.	Bialk-Bielinska et al. 2011
Animal feeds **HPLC** **Fluorometric detection** **Precolumn derivatization**	Two analytical methodologies for the simultaneous analysis of eight sulfonamide antibiotics in animal feeds were developed. Analytes were extracted in a simple and rapid procedure by manual shaking with an ethyl acetate/ultrapure water mixture (99:1, v/v) without further sample cleanup. Mean recoveries ranging from 72.7% to 99.4% with relative standard deviations below 9% were achieved from spiked animal feed samples. Determination was carried out by high-performance liquid chromatography using fluorometric detection with precolumn derivatization. The separation of the derivatized compounds was performed using two different chromatographic columns: a conventional C_{18} column and a recently available core-shell particle Kinetex C_{18} column. Both methods were validated in-house in six different feed matrices, and the two approaches were compared. The experiments showed that the method using the Kinetex column was superior with regard to speed of analysis and precision, both under repeatability and intermediate reproducibility conditions. The limits of detection and quantification were also greatly improved, below 0.10 and 0.34 μg respectively. Finally, this novel approach was successfully applied to the analysis of real feed samples.	Borras et al. 2011
Sewage treatment plants **Review on methods**	A large number of xenobiotics including pharmaceuticals and personal care products are continuously released into the environment. Effluents from sewage treatment plants are well known to be the major source for introduction of pharmaceuticals and personal care products into the aquatic system. In recent years, reliable methods have been established for residue analysis of these pollutants down to low ng/l levels. In this review, the different approaches to their trace determination are reviewed with special attention being paid to sample preparation procedures, state-of-the-art high-performance separation methods hyphenated with mass spectrometry, and immunochemical methods.	Buchberger 2011

ANALYSIS		
Wastewater treatment plants **Sewage sludge** **Biosolid** **Solvent extraction** **LC-MS/MS**	An analytical method was developed to quantitatively determine pharmaceuticals in biosolid (treated sewage sludge) from wastewater treatment plants (WWTPs). The collected biosolid samples were initially freeze dried, and grounded to obtain relatively homogenized powders. Pharmaceuticals were extracted using accelerated solvent extraction (ASE) under the optimized conditions. The optimal operation parameters, including extraction solvent, temperature, pressure, extraction time and cycles, were identified to be acetonitrile/water mixture (v/v 7 : 3) as extraction solvent with three extraction cycles (15 min for each cycle) at 100 degrees C and 100 bars. The extracts were cleaned up using solid-phase extraction followed by determination by liquid chromatography coupled with tandem mass spectrometry. For the 15 target pharmaceuticals commonly found in the environment, the overall method recoveries ranged from 49% to 68% for tetracyclines, 64% to 95% for sulfonamides, and 77% to 88% for other pharmaceuticals (i.e. acetaminophen, caffeine, carbamazepine, erythromycin, lincomycin and tylosin). The developed method was successfully validated and applied to the biosolid samples collected from WWTPs located in six cities in Michigan. Among the 15 target pharmaceuticals, 14 pharmaceuticals were detected in the collected biosolid samples. The average concentrations ranged from 2.6 μg/kg for lincomycin to 743.6 μg/kg for oxytetracycline. These results indicated that pharmaceuticals could survive wastewater treatment processes, and accumulate in sewage sludge and biosolids. Subsequent land application of the contaminated biosolids could lead to the dissemination of pharmaceuticals in soil and water environment, which poses potential, threats to at-risk populations in the receiving ecosystems.	Ding et al. 2011
Groundwater **SPE-LC-ESI-MS/MS**	The present study describes an automated methodology based on a liquid chromatography-electrospray, tandem mass spectrometry method combined with online solid phase extraction (online SPE-LC-ESI-MS/MS) for the simultaneous analysis of 16 sulfonamides (SAs) and five of their acetylated metabolites in groundwater. The evaluation of the degree of SA pollution in groundwater was made through the analysis of a total of 39 samples taken in seven groundwater bodies of Catalonia (Spain). Recovery values obtained ranged from 34.3% (N_4-acetylsulfadiazine) to 134.4% (sulfabenzamide). The method limits of detection for all the analytes were 0.09–11 ng/l. Sulfamethoxazole was the SA detected more frequently (56.4% of the samples), with an average concentration of 2.3 ng/l, followed by sulfadimethoxine, present in 54% of the samples with an average concentration of 0.2 ng/l. It should be highlighted that the acetylated metabolites were ubiquitous in the different samples, with frequencies of detection up to 36% and maximum concentrations of 18 ng/l (N_4-acetylsulfamerazine).	Garcia-Galan et al. 2011c
Shrimp **HPLC/MS/MS** **Multiclass/multiresidue method**	A multiclass/multiresidue method has been developed and validated for the determination of 21 veterinary drug residues in shrimp, including sulfonamides (sulfadiazine, sulfamerazine, sulfamethazine, sulfachloropyridazine, sulfadimethoxine, and sulfaquinoxaline); tetracyclines (oxytetracycline, tetracycline, and chlortetracycline); (fluoro)quinolones (norfloxacin, ciprofloxacin, enrofloxacin, sarafloxacin, difloxacin, flumequine, oxolinic acid, and nalidixic acid); and cationic dyes (malachite green, gentian violet, leucomalachite green, and leucogentian violet), using HPLC/MS/MS. All drugs were quantifiable over a no less than 10-fold range with matrix-matched standards for linear external calibration, except for oxytetracycline, tetracycline, norfloxacin, and ciprofloxacin, for which norfloxacin-d(5) was used as an internal standard. Two grams of preground shrimp sample was extracted twice with extractant at two different pH values. The combined supernatant was further diluted with an aqueous internal standard solution, and 50 μl extract was injected into the HPLC instrument. An online SPE system was set up for automated sample cleanup. A triple quadrupole mass spectrometer equipped with an electrospray ionization source was operated in the multiple-reaction-monitoring mode to acquire data. The method has been validated at three levels within the designated linear ranges for each drug, with accuracies between 77 and 115%, and most CV values below 15%.	Li and Kijak 2011

Hospital efluent water **LS-MS**	In this work, an analytical methodological study was carried out to determine the antimicrobials sulfamethoxazole and trimethoprim, as well as their metabolites, in hospital effluent. The determinations were conducted by liquid chromatography tandem mass spectrometry using a hybrid triple quadrupole-linear ion trap mass spectrometer (LC-QqLIT-MS). The data acquisition was made in selected reaction monitoring (SRM) mode, in which two SRM transitions were monitored to ensure that the target compounds were accurately identified by the information dependent acquisition (IDA) function. The limits of detection (LOD) and quantification (LOQ) were 0.25 and 0.80 µg/l for sulfamethoxazole and 0.15 and 0.50 µg/l for trimethoprim. The linear range for the SMX was 0.8–100.0 µg/l and TMP was 0.5–100.0 µg/l on the basis of six-point calibration curves generated by means of linear regression analysis. The coefficients of the correlation were higher than 0.999, which ensured the linearity of the method. The average concentration of sulfamethoxazole and trimethoprim found in hospital effluent was 27.8 and 6.65 µg/l, respectively. The analytical methodology employed allowed two metabolites to be identified, N4-acetyl-sulfamethoxazole and alpha-hydroxy-trimethoprim.	Brenner et al. 2011
Sea water **SPE, LC-MS/MS** **36 residues**	We have therefore developed a method for the rapid detection of 36 antibiotic residues in coastal waters, including tetracyclines (TCs), sulfanilamides (SAs), and quinolones (QLs). The method consists of solid-phase extraction (SPE) and liquid chromatography-tandem mass spectrometry (LC-MS/MS) analysis, using electrospray ionization (ESI) in positive mode. The SPE was performed with Oasis HLB and Oasis MCX cartridges. Chromatographic separation on a C18 column was achieved using a binary eluent containing methanol and water with 0.1% formic acid. Typical recoveries of the analytes ranged from 67.4% to 109.3% at a fortification level of 100 ng/l. The precision of the method, calculated as relative standard deviation (RSD), was below 14.6% for all the compounds. The limits of detection (LODs) varied from 0.45 pg to 7.97 pg. The method was applied to determine the target analytes in coastal waters of the Yellow Sea in Liaoning, China. Among the tested antibiotics, 31 were found in coastal waters, with their concentrations between the LOD and 212.5 ng/l. These data indicate that this method is valid for analysis of antibiotics in coastal waters. The study first reports such a large number of antibiotics along the Yellow Sea coast of Liaoning, and should facilitate future comprehensive evaluation of antibiotics in coastal ecosystems.	Na et al. 2011
Pharmaceuticals **Differential pulse voltammetry** **Five sulfonamides**	The electrochemical behaviours of five sulfonamides (sulfanilamide, sulfadiazine, sulfamerazine, sulfamonomethoxine, sulfamethoxazole) were investigated with overoxidized polypyrrole (OPPy) modified pencil graphite electrodes. The performance of the OPPy electrode was evaluated by differential pulse voltammetry in Britton-Robinson buffer solutions prepared in different ratio of acetonitrile-water binary mixture, between pH 1.5 and 7.0. The highest anodic signals of sulfonamides were obtained in Britton-Robinson buffer solution prepared in 50% (v/v) acetonitrile-water at pH 2.5 and 3.0. The OPPy electrodes exhibited good performance for sulfonamides with wide linear ranges (approximate to 10^{-5}–10^{-3} M), highly reproducible responses (RSD% ≤ 0.92) and correlation coefficients (≥ 0.9990). The calculated limits of detection were similar to 10^{-6} or 10^{-7} M at 3 sigma. In order to verify the reliability of the OPPy electrode as a sensor, it is used for determination of sulfamethoxazole in a pharmaceutical tablet. The recovery was found as 95.96% with the RSD% of 0.68. The overoxidized polypyrrole modified pencil graphite electrode showed a stable and reproducible response without any influence of interferent commonly existing in pharmaceutical containing sulfamethoxazole.	Ozkorucuklu et al. 2011
Microwave-assisted extraction **HPLC-MS** **Manure**	A novel method entailing microwave-assisted extraction (MAE) and high-performance liquid chromatography-electrospray mass spectrometry (LC-MS (n)) has been developed for determination of selected typical antibiotics, including quinolones, sulfonamides, and tetracyclines, in manure. Compared with ultrasonic extraction, MAE significantly increased recovery of fluoroquinolones (63–106%), sulfonamides (64–133%), and tetracyclines (64–109%) from manure. Acetonitrile acidified with formic acid buffer solution (pH 4.0) was used for extraction of swine manure whereas chicken manure was extracted with 0.1 M EDTA-McIlvaine buffer solution. Limits of quantification (LOQ) for all compounds were in the range 5.12–168.4 µg/kg dry matter, which were satisfactory for analysis of all samples. The suitability of the method was assessed by analysis of manure from six different sites.	Hu et al. 2010

ANALYSIS		
Swine wastewater **Suspended solids** **SPE, LC-MS**	A method for simultaneous determination of three classes of veterinary antibiotics in the suspended solids (SS) of swine wastewater, including five sulfonamides, three tetracyclines and one macrolide (tiamulin). The entire procedures for sample pretreatment, ultrasonic extraction (USE), solid-phase extraction (SPE), and liquid chromatography-mass spectrometry (LC-MS) quantification were examined and optimized. The recovery efficiencies were found to be 76%–104% for sulfonamides, 81%–112% for tetracyclines, and 51%–64% for tiamulin at three spiking levels. The intra-day and inter-day precisions, as expressed by the relative standard deviation (RSD), were below 17%. The method detection limits (MDLs) were between 0.14 and 7.14 μg/kg, depending on a specific antibiotic studied. The developed method was applied to field samples collected from three concentrated swine feeding plants located in Beijing, Shanghai and Shandong province of China. All the investigated antibiotics were detected in both SS and liquid phase of swine wastewater, with partition coefficients (logK(d)) ranging from 0.49 to 2.30. This study demonstrates that the SS cannot be ignored when determining the concentrations of antibiotics in swine wastewater.	Pan et al. 2011b
Water **Hollow fiber-based liquid phase microextraction** **HPLC** **Diode array** **Fluorescence detection**	Three phase-hollow fiber-based liquid phase microextraction (HF-LPME) combined with a HPLC procedure using diode array (DAD) and fluorescence detection (FLD) has been developed for the determination of four widely used sulfonamides: sulfadiazine, sulfamerazine, sulfamethazine, sulfamethoxazole and their main metabolites, the corresponding N-4-acetyl derivatives: N-4-acetyl-sulfadiazine, N-4-acetyl-sulfamerazine, N-4-acetyl-sulfamethazine, N-4-acetyl-sulfamethoxazole. A Q3/2 Accurel KM polypropylene hollow fiber supporting 1-octanol was used between a 2M Na_2SO_4 aqueous solution (pH 4) as a donor phase and aqueous solution (pH 12) as an acceptor phase. The procedure allows very low detection and quantitation limits of 0.3–33 ng/l and 0.9–100 ng/l, respectively. The proposed method was applied to the determination of the analytes in environmental water samples (surface, tap and wastewater).	Payan et al. 2011
Multianaylysis (33 analyts) **SPE, LC/MS-MS**	This paper describes the presence of 33 pharmaceuticals and hormones in waters from two sewage treatment plants (STPs) situated in Catalonia, in northeastern Spain. The target compounds were one psychoactive stimulant, one antiepileptic, four analgesics and non-steroidal anti-inflammatories, one lipid regulators, two anti-ulcer agents, nine antibiotics (sulfonamides and macrolides), two beta-blockers, two metabolites, and 11 hormones (free and conjugates). The determination was performed using liquid chromatography coupled to tandem mass spectrometry after enrichment by solid-phase extraction with Oasis HLB sorbent. Most of the pharmaceuticals were found in both influent and effluent samples from the two STPs. The most frequently detected were caffeine, acetaminophen, carbamazepine, diclofenac, ibuprofen, naproxen, sulfamethoxazole, sulfapyridine, sulfathiazole, ranitidine, omeprazole, estrone 3-sulfate, and estradiol 17-glucuronide. Specifically, the highest concentrations found in influents were 19 850 ng/l (acetaminophen), 9945 ng/l (caffeine), 4215 ng/l (ibuprofen), 5695 ng/l (sulfamethoxazole), and 5140 ng/l (sulfathiazole). Most of the pharmaceuticals present in influent waters were found in effluents at lower concentrations. The highest concentrations in effluents were 970 ng/l (caffeine), 670 ng/l (sulfamethoxazole), 510 ng/l (bezafibrate), and 1032 ng/l (diclofenac).	Pedrouzo et al. 2011
Water and soil **Solid-phase extraction** **Multiple analytes monitoring** **LC-MS**	This method for analyzing free (parent estrogen) and conjugated estrogens (metabolites) along with sulfonamides and tetracyclines utilizes a high pH (10.4) mobile phase with an ammonium hydroxide buffer for both positive- and negative-mode electrospray ionization. A single-step sample preparation by solid-phase extraction (SPE) was used to isolate and concentrate all analytes simultaneously. The analytical method was developed and validated for recoveries at 3 concentration levels for water and soil and produced recoveries of 42–123% and 21–105% respectively. Method detection limits ranged from 0.3 to 1.0 ng/l for water samples and 0.01 to 0.1 ng/g for soils. The method quantification limit ranged from 0.9 to 3.3 ng/l for water samples and 0.06 to 0.7 ng/g for soils. This method has been used for the quantification of estrogens, tetracyclines, and sulfonamides in soil and runoff waters with multiple compounds detected simultaneously in a single analysis.	Tso et al. 2011

Water **Ionic liquid-based single drop microextraction** **HPLC** **Sulfonamides**	A novel method was developed for the determination of seven sulfonamides in water samples using ionic liquid-based single drop microextraction coupled with high performance liquid chromatography. The influence of extraction parameters including extraction solvent, volume of extraction solvent, extraction time, stirring speed, pH value, NaCl concentration of sample solution and extraction temperature were investigated. Using 9 µl-butyl-3-methylimidazolium hexafluorophosphate ([C_4MIM][PF_6]) as extraction drop, 10.0 ml aqueous sample with 0.33 g/ml NaCl (pH 3) was extracted for 35 min with stirring at 300 r/min at 50 degrees C. Under the optimal conditions, good linear relationships were obtained in the sulfonamides concentrations of 0.005–2.000 mg/l with the correlation coefficients of 0.9994–0.9998; the detection limits were 0.001–0.003 mg/l (S/N = 3); the enrichment factors of [C_4MIM][PF_6] for the seven sulfonamides were from 22 to 107; the RSD of matrix spiked samples were 3.1%–5.6% (n = 5). The proposed method was applied to the determination of the seven sulfonamides in tap, river, lake and waste water with recoveries of the seven sulfonamides in the range of 84.3%–106.0%.	Wu et al. 2011
Aqueous two-phase system **HPLC** **Sulfamethoxazole**	Based on the poly(propylene glycol)(400)(PPG(400)-salt aqueous two-phase system (ATPS), a green, economical and effective sample pretreatment technique coupled with high performance liquid chromatography was proposed for the separation and determination of sulfamethoxazole (SMX). The extraction yield of SMX in PPG(400)-salt ATPS is influenced by various factors, including the salt species, the amount of salt, pH, and the temperature. Under the optimum conditions, most of SMX was partitioning into the polymer-rich phase with the average extraction efficiency of 99.2%, which may be attributed to the hydrophobic interaction and salting-out effect. This extraction technique has been successfully applied to the analysis of SMX in real water samples with the recoveries of 96.0–100.6%, the detection limits of 0.1 µg/l, and the linear ranges of 2.5–250.0 µg/l.	Xie et al. 2011
Waste water **Ground water** **Surface water** **19 sulfonamides** **SPE-LC-MS/MS**	The present study describes the development, validation and a practical application of a fully automated analytical method based on on-line solid-phase extraction-liquid chromatography-tandem mass spectrometry (SPE-LC-MS/MS) for the simultaneous determination of 19 sulfonamides, including one acetylated metabolite, in different water matrices. MS/MS detection was carried out in a quadrupole-linear ion trap (QqLIT) mass analyzer. Target compounds were identified in the selected reaction monitoring (SRM) mode, recording two transitions between precursor ions and the two most abundant product ions. The method developed was applied to evaluate the occurrence of the target antibiotics in different water samples: influent and effluent water from waste water treatment plants (WWTP), ground water and surface water. Under optimal conditions, the method detection limits achieved were in the range 0.05–7.84 ng/l for WWTP influent water, 0.01–6.90 ng/l for WWTP effluent water, 0.02–5.13 ng/l for ground water and 0.02–4.52 ng/l for surface water samples. The instrumental repeatability, expressed as RSD, was usually below 10% for the different water matrices. Results showed the wide presence of sulfonamides in the four types of water, including one acetylated metabolite, with maximum concentrations up to 855 ng/l corresponding to sulfapyridine in an influent waste water sample near a densely populated urban area.	Garcia-Galan et al. 2010a, b
Immuno-chromatography **Chicken breast, eggs**	A rapid and sensitive immunochromatographic assay (ICA) based on competitive format was developed and validated for simultaneous detection of sulfamethazine (SM2), sulfadiazine (SDZ), and sulfaquinoxaline (SQX) in chicken breast muscle and egg samples. For this purpose, three monoclonal antibodies raised against those three sulfonamides were conjugated to colloidal gold particles and applied to the conjugate pads of the test strip. The competitors of the sulfonamides (SM2/SDZ/SQX-bovine serum albumin conjugates) were immobilized onto a nitrocellulose membrane at three detection zones to form T-1, T-2, and T-3, respectively. With this method, the cutoff values for the three test lines were achieved at 80 µg/kg, which is lower than the maximum residue levels (MRLs) established for sulfonamides. The recoveries in negative samples spiked at concentrations of 10, 50, and 100 µg/kg ranged from 75% to 82% for egg samples and from 78% to 81% for chicken samples. The method was compared with the HPLC method by testing 180 eggs and chicken breast samples from local markets, and an agreement rate of 99.7% was obtained between the two methods.	Guo et al. 2010

ANALYSIS		
Immunosensors **Sulfathiazole** **Water – no sample treatment** **Honey after SFE**	The development of two sensitive and selective immunosensors for sulfathiazole, using immunoreagents – haptens, polyclonal antibodies, enzyme conjugates – previously obtained and characterized, is presented One of them is based on the competitive immunocomplex capture format making use of an immobilized protein A/G sorbent, while the other employs a restricted access support in a novel homogeneous-heterogeneous (HH) assay mode. Maximum sensitivity, achieved with a total assay time of 18 min for the capture sensor, is traduced in a dynamic range from 0 4 to 24 μg/l with a lower limit of detection of 0.11 μg/l. Increasing to 1.2 μg/l when employing an accelerated capture assay protocol that yields a sampling rate of 7 cycles per hour. The HH sensor shows the fastest response, performing each whole assay in only 2 min, with a limit of detection of 0.85 and a measurement interval of 3.9–181.0 μg/l, and with no need of support regeneration. Immunosensors are selective for sufathiazole, and only sulfamethoxypyridazine, sulfamethizole and sulfapyridine show non-negligible cross-reactivity, the same as in ELISA batch immunoassay. The application of the developed systems to the analysis of water, with no sample treatment, as well as honey samples after solid-phase extraction, demonstrate the reliability of the immunosensing for the monitoring of this type of pollutants.	Jornet et al. 2010
Soil **Different extraction methods**	The extraction of six sulfonamides (sulfadiazine, sulfadimidine, sulfathiazole, sulfachloropiridazine, sulfadimethoxine, and sulfaquinoxaline) from soils with different physicochemical characteristics and at several aging times was investigated. Conventional mechanical shaking, microwave-assisted extraction, ultrasound probe-assisted extraction and pressurized liquid extraction techniques were evaluated. The four techniques provided similar results when applied to freshly contaminated soils. However, microwave-assisted extraction was the most suitable to extract sulfonamide aged residues from soils. Microwave-assisted extraction was applied to eight soils aged for three months, using acetonitrile: buffer pH 9 (20:80) as the extraction solvent, and recoveries ranged from 15–25% for STZ to 42–64% for SDM.	Raich-Montiu et al. 2010
Soil **Slurry manure** **UHPLC-TQ-MS/MS** **14 sulfonamides**	An analytical method was developed using ultra-high-pressure liquid chromatography-triple quadrupole-tandem mass spectrometry (UHPLC-TQ-MS/MS) to simultaneously analyze 14 sulfonamides (SA) in 6 min. Despite the rapidity of the assay the system was properly re-equilibrated in this time. No carryover was observed even after high analyze concentrations. The instrumental detection limit based on signal-to-noise ratio (S/N) > 3, was below 1 pg/μl (5 pg on column) for all SAs except sulfachloropyridazine. Surface water, ground water, soil and slurry manure contained in storage ponds in and around swine rearing facilities were analyzed. Sample cleanup for ground water and surface water included using solid phase extraction (SPE) using Oasis® hydrophilic-lipophilic balance (HLB) cartridges. The soil and slurry manure required tandem strong anion exchange (SAX) and HLB solid phase extraction cartridges for sample cleanup. With few exceptions, the recoveries ranged from 60 to 100% for all matrices. The minimum detectable levels were below 20 ng/l for water, 30 ng/l for slurry manure, and 45 ng/kg for soil except for sulfachloropyridazine. The coefficient of variation (CV) was within 20% for most of the compounds analyzed. Using this method, sulfamethazine concentrations of 2250–5060 ng/l, sulfamethoxazole concentrations of 108–1.47 × 10^6 ng/l, and sulfathrazole concentrations of 785–1700 ng/l were found in the slurry manure sulfadimethoxine (2.0–32 ng/l), sulfamethazine (2.0–5.1 ng/l). and sulfamethoxazone (20.5–43.0 ng/l) were found In surface water and ground water In topsoil (0–15 cm), sulfamethazine ranged 34.5–663 ng/kg dry weight in those locations that received slurry manure as a nutrient, no SAs were found in the soil depths between 46 and 61 cm.The speed makes the method practical for medium to high throughput applications. The sensitivity and positive analyse identification make the method suitable for the demanding requirements for real world applications.	Shelver et al. 2010

Soil **Microwave-assisted extraction**	A rapid technique based on dynamic microwave-assisted extraction (DMAE) coupled on-line with solid-phase extraction (SPE) was developed for the determination of sulfonamides (SAs) including sulfadiazine, sulfameter, sulfamonomethoxine and sulfaquinoxaline in soil. The SAs were first extracted with acetonitrile under the action of microwave energy, and then directly introduced into the SPE column which was packed with neutral alumina for preconcentration of analytes and clean-up of sample matrix. Subsequently, the SAs trapped on the alumina were eluted with 0.3% acetic acid aqueous solution and determined by liquid chromatography-tandem mass spectrometry. The DMAE parameters were optimized by the Box-Behnken design. Maximum extraction efficiency was achieved using 320 W of microwave power; 12 ml of extraction solvent and 0.8 ml/min of extraction solvent How rate. The limits of detection and quantification obtained are in the range of 1.4–4.8 ng/g and 4.6–16.0 ng/g for the SAs, respectively. The mean values of relative standard deviation of intra- and inter-day ranging from 2.7% to 5.3% and from 5.6% to 6.7% are obtained, respectively. The recoveries of SAs obtained by analyzing four spiked soil samples at three fortified levels (20 ng/g, 100 ng/g and 500 ng/g were from 82.6 ± 6.0% to 93.7 ± 5.5%. The effect of standing time of spiked soil sample on the SAs recoveries was examined. The recoveries of SAs decreased from (86.3–101.9)% to (37.6–47.5)% when the standing time changed from one day to four weeks.	Chen et al. 2009
Sulfamethoxazole **ELISA** **Screening**	Different immunoassays have been developed to monitor sulfamethoxazole (SMX), an antibiotic frequently detected in water. The immunoassays were developed and optimized in two different formats: ELISA in polystyrene 96-well plate and microarray on compact disc (CD) support. Competitive microimmunoassays were performed by direct adsorption of immunoreagents on the polycarbonate surface of a low-reflectivity CD. Results were displayed using nanogold-labeled immunoglobulins and silver staining developer. High sensitivity was achieved with both formats: LD 0.001 ng/ml in the ELISA-plate, and 0.09 ng/ml in the CD format. The novel CD methodology presents advantages such as simplicity, sensitivity, portability, analytical capacity (2560 spots per disc), in addition to reductions in immunoreagents required, costs and time for analysis. Both proposed methods were applied to determine SMX at nanograms per litre level in wastewater samples without previous preconcentration. Finally, the determination of several fortified wastewater samples using the CD format protocol showed a mean recovery of 87%, which confirms that this assay format is a good screening tool to detect sulfamethoxazole in water samples rapidly and reliably.	Pastor-Navarro et al. 2009
Swine waste water **Lake water** **Ground water** **China** **SPE-LC/MS/MS**	Strategies for sample preparation. solid-phase extraction (SPE), clean-up, and detection conditions of an optimized solid-phase extraction-liquid chromatography/mass/mass spectrometry (SPE-LC/MS/MS) method for determining multi-residues of four classes of widely used antibiotics in pig farms, sulfonamides (SAs), fluoroquinolone (FQs), tetracycline (TCs) and chloramphenicol (CAP) were presented. The multi-residue analysis was used in MS analysis, selecting two precursor ions to produce ion transitions for each target compound. Samples of swine wastewater, lake water and groundwater collected from two pig farms in central China were used to test the applicability of the multi-residue analysis method. The average antibiotics concentrations in groundwater, lake water, final effluent and influent swine wastewater were, respectively, 1.6–8.6, 5.7–11.6, 7.9–1172.3 and 8.5–21 692.7 ng/l in summer; respectively, 2.0–7.3, 6.7–11.7, 5.8–409.5 and 32.8–11 276.6 ng/l in winter. The limits of quantification were 0.8–4.1, 1.4–5.5, 1.8–11.5 and 6.4–104.4 ng/l, respectively, in groundwater, lake water, final effluent and influent swine wastewater. Results of multi-residue analysis of antibiotics in the samples indicate that SAs, FQs and TCs were widely used veterinary medicines in the pig farms. As compared with previous studies, higher elimination rates (more than 80%) of the antibiotics (except DC) were observed in effluent in this study. More detailed work is indispensable to investigate the fate and transport of antibiotics in the environment and to find out cost-effective approaches of removing antibiotics from swine wastewater and contaminated sites.	Tong et al. 2009

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