Journal of Environmental Management 217 (2018) 629–645

Contents lists available at ScienceDirect

Journal of Environmental Management

journal homepage: www.elsevier.com/locate/jenvman

Review

A review of analytical procedures for the simultaneous determination of medically important veterinary antibiotics in environmental water: Sample preparation, liquid chromatography, and mass spectrometry

Chansik Kim, Hong-Duck Ryu, Eu Gene Chung*, Yongseok Kim, Jae-kwan Lee

Department of Water Environment Research, National Institute of Environmental Research, Hwangyeong-ro 42, Seo-gu, Incheon, 22689, South Korea

A R T I C L E I N F O

Article history:
Received 23 August 2017
Received in revised form
10 March 2018
Accepted 2 April 2018

Keywords:
Veterinary antibiotics
Medically important antibiotics
Antibiotic sales
Solid-phase extraction
HPLC-MS/MS

A B S T R A C T

Medically important (MI) antibiotics are defined by the United States Food and Drug Administration as drugs containing certain active antimicrobial ingredients that are used for the treatment of human diseases or enteric pathogens causing food-borne diseases. The presence of MI antibiotic residues in environmental water is a major concern for both aquatic ecosystems and public health, particularly because of their potential to contribute to the development of antimicrobial-resistant microorganisms. In this article, we present a review of global trends in the sales of veterinary MI antibiotics and the analytical methodologies used for the simultaneous determination of antibiotic residues in environmental water. According to recently published government reports, sales volumes have increased steadily, despite many countries having adopted strategies for reducing the consumption of antibiotics. Global attention needs to be directed urgently at establishing new management strategies for reducing the use of MI antimicrobial products in the livestock industry. The development of standardized analytical methods for the detection of multiple residues is required to monitor and understand the fate of antibiotics in the environment. Simultaneous analyses of antibiotics have mostly been conducted using high-performance liquid chromatography–tandem mass spectrometry with a solid-phase extraction (SPE) pretreatment step. Currently, on-line SPE protocols are used for the rapid and sensitive detection of antibiotics in water samples. On-line detection protocols must be established for the monitoring and screening of unknown metabolites and transformation products of antibiotics in environmental water.

Contents

* Corresponding author.
E-mail address: egchung@korea.kr (E.G. Chung).

https://doi.org/10.1016/j.jenvman.2018.04.006
0301-4797/

1. Introduction

Demands for animal protein are steadily increasing, especially in low- and middle-income countries owing to the improvements in their standards of living (Tilman et al., 2011). For instance, the daily intake of animal protein in Asia has increased from 7 g/capita to 25 g/capita between 1960 and 2013 (Van Boeckel et al., 2015), with a concomitant increase in GDP per capita from $300 to $16,100, over the same period (The World Bank, 2017). Brazil, Russia, India, China, and South Africa (BRICS; an international association of major emerging economies) have expanded their investments in the intensive livestock-production industry in response to the global growth of both the meat and animal-protein markets. These markets rely on the use of large amounts of veterinary antibiotics in order to prevent infectious diseases and to improve the productivity of livestock in concentrated animal-feeding operations (CAFOs).

Since animals usually excrete 30–90% of parent compounds delivered to their bodies orally, through feed and water, or by injection (Alcock et al., 1999; Kumar et al., 2005; Montforts, 1999; Sukul et al., 2009), antibiotics and their metabolites are consequently introduced into the aqueous environment via animal excreta (Martínez-Carballo et al., 2007; Zhao et al., 2010), composted manure (Bak et al., 2013; Sarmah et al., 2006), and/or wastewater from CAFOs (Andersson and Hughes, 2014). Inappropriate disposal of antibiotics in rearing farms is also a major cause of surface-water contamination (Dasgupta and Sengupta, 2015). The detection of various antibiotics at levels of several hundred mg/kg in livestock excreta was reported (Jacobsen and Halling-Sørensen, 2006; Martínez-Carballo et al., 2007; Zhao et al., 2010) and some of the antibiotics detected did not decompose during manure composting. Dolliver et al. (2008) evaluated the degradation of monensin, sulfamethazine, and tylosin during a composting period of 22–35 days, and observed no degradation of sulfamethazine and only partial (54–76%) decomposition of the others. Schlüsener et al. (2006) monitored the concentrations of four veterinary antibiotics in a liquid manure tank for 180 days and calculated the half-life of each compound. Salinomycin, erythromycin, and roxithromycin showed first-order degradation with half-lives of 6, 41, and 130 days, respectively; no degradation of tiamulin was observed. Hence, composted manure with animal excreta may contain antibiotic residues when applied to crop farmlands as organic fertilizers.

Some antibiotic residues can impact negatively both the aquatic ecosystem and human health, even at low ng/L levels, by inhibiting cell reproduction and growth (Liu and Wong, 2013; Malchi et al., 2014; Rahman et al., 2009). Trimethoprim, enrofloxacin, ciprofloxacin, sulfaquinoxaline, monensin, narasin, and salinomycin are well known antimicrobials that cause toxicity to freshwater microalgae (cyanobacteria), aquatic and soil organisms, and fish (González-Pleiter et al., 2013; Isidori et al., 2005; Jung et al., 2008; Kim and Aga, 2007; Madureira et al., 2011; Robinson et al., 2005; Wollenberger et al., 2000). The phytotoxicties of enrofloxacin and ciprofloxacin to crop plants have also been reported by Migliore et al. (2003), while Pomati et al. (2008) identified the effects of pharmaceutical mixtures on *Escherichia coli* (*E. coli*), human embryonic HEK293 kidney cells, and estrogen-responsive OVCAR3 tumor cells using *in vitro* cytotoxicity testing. Atenolol, bezafibrate, ciprofloxacin, and lincomycin were identified as posing potential hazards to infants and pregnant women exposed to contaminated drinking water. Drug mixtures were also found to be significantly toxic at environmentally relevant exposure levels (ng/L) as a result of synergisms between components in the mixtures (Aga et al., 2016; Marx et al., 2015; Pomati et al., 2008).

Bacterial antibiotic resistance is a serious public health issues (Landers et al., 2012). Continuous exposure to antibiotics in the environment has led to the development of antibiotic resistance in microorganisms, and infections caused by antibiotic-resistant bacteria can be difficult, or sometimes impossible, to cure. The emergence of antibiotic-resistant bacteria has been reported since the early 1990s, and has led to the development of new generations of antibiotics over the past few decades (Bonnet, 2004; Fischbach and Walsh, 2009; Hasman et al., 2005; Hur et al., 2012; Neu, 1992; Straus and Hancock, 2006). For example, some penicillins and cephalosporins (prescribed for patients allergic to penicillin) are ineffective against extended-spectrum β-lactamase-producing bacteria (Dutil et al., 2010; Franciolli et al., 1991; Jones, 2001; Pfeifer et al., 2010). Bacterial resistance to these antibiotics had led to the frequent use of carbapenem antibiotics as alternatives (Bhavnani et al., 2006; Hawkey and Livermore, 2012); however, carbapenem-resistant Enterobacteriaceae was observed immediately (Nordmann et al., 2011, 2012). Antibiotic-resistant microorganisms capable of causing severe infections have been found ubiquitously and are easily spread through wastewater and sludge (Biswal et al., 2014; Chen and Zhang, 2013), water recreation parks (Santiago-Rodriguez et al., 2013), aquaculture farms (Gao et al., 2012b), and foods of animal origin (Carretero et al., 2008; Mathew et al., 2007; Wan et al., 2006; Xu et al., 2012). The United States Center for Disease Control and Prevention (CDC) (2013) has estimated that at least two million people became ill, and 23,000 died every year as a consequence of antibiotic-resistant infection in the United States. The development of resistance is directly linked with the levels of antibiotic use, and, thus, it is desirable to minimize the sales of antibiotics for the treatment of animal diseases by avoiding misuse and overuse. Chantziaras et al. (2014) presented a correlation between antimicrobial use and the prevalence of resistance in *Escherichia coli* isolated from pigs, poultry, and cattle, and demonstrated a strong linear relationship based on data from seven European countries (Norway, Sweden, Denmark, Austria, Switzerland, Netherlands, and Belgium).

In order to minimize the generation of antibiotic resistant bacteria, the United States Food and Drug Administration (FDA) (2003) has identified specific active antimicrobial ingredients as “medically important” (MI) and essential components in the treatment of human diseases or enteric pathogens (Table S1). In addition, the World Health Organization (WHO) (2012) has categorized particular antibiotic classes that are used solely in therapies, or are