LC–MS^2 for quantifying trace amounts of pharmaceutical compounds in soil and sediment matrices

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The occurrence of pharmaceuticals in watersheds has recently received increased attention due to the possibility of adverse effects on humans and animals and potential development of resistance genes in bacteria. Human and veterinary pharmaceuticals can be introduced into the environment through several different pathways, depending on usage patterns, hydrology and treatment practices. However, limited information about the occurrence and the fate of pharmaceuticals in the environment is available and, as a result, efficient mitigation strategies have been difficult to define. Robust, reliable methods therefore need to be developed to measure human-origin or veterinary pharmaceuticals at environmentally relevant concentrations in aqueous and solid matrices. Solid-phase extraction coupled with high-performance liquid chromatography mass spectrometry or tandem mass spectrometry has been utilized to pre-treat, separate, and detect the residuals of pharmaceuticals in a wide range of environmental samples. This article reviews the recent development of analytical methods for quantifying pharmaceutical residues in a range of solid matrices found in the environment.

Keywords: High-performance liquid chromatography; HPLC–MS^2; Mass spectrometry; PEC; Pharmaceuticals; Predicted environmental concentration; Soil; Sediment

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1. Introduction

Pharmaceuticals, including antibiotics, antiphlogistics, lipid regulators and β-blockers, have received significant attention in the environmental field recently due to the detection of these compounds in a variety of matrices (e.g., surface water, groundwater, soil, and sediment). Pharmaceuticals are used to abate bacterial infection for humans. They are used not only to prevent illness but also to promote growth of animals [1,2].

Based on pharmacokinetic data, the excretion rate of pharmaceuticals is sometimes over 50% as the parent compound or metabolites. Metabolites may conjugate with glucose or other polar compounds and be converted to the original parent compound in the environment with microorganism activity [3]. The estimated annual weights of antimicrobials used in the USA for therapeutic purposes in humans and animals are 3 million pounds and 2 million pounds, respectively. Meanwhile, the annual consumption in animals for non-therapeutic purposes, mainly as growth promoters, is about 25 million pounds [4]. Thus, it is not surprising that residuals of pharmaceutical compounds can be found in a wide range of environmental matrices.

Another problem with persistent pharmaceuticals in the environment is the possibility of producing resistance genes in bacteria that can render particular antibiotics useless. Resistance mechanisms are often related to transposons or conjugative plasmids as mobile genetic elements and those elements can transfer the resistance genes from one bacteria to another through horizontal gene transfer [5]. Among other pharmaceuticals, resistance genes of tetracycline have been reported in lagoons and the groundwater underlying two swine-production facilities [6]. In addition, the ecotoxicity of doxycycline in aged pig manure was assessed using a multi-species soil system and the tolerance of the soil microbial communities affected by sulfachloropyridazine was investigated [7,8].

Despite the fact that numerous pharmaceuticals have been found in environmental matrices, there is still a lack of

0165-9936/$ - see front matter doi:10.1016/j.trac.2005.04.006

robust, reliable analytical methods for quantifying the pharmaceuticals in realistic matrices at environmentally relevant concentrations. Consequently, the need for continued development of analytical methods is among the highest priorities in the field. In particular, there is a need for development and description of analy- tical methods in solid matrices, such as soil and sediment.

This article reviews analytical methods for quantifying pharmaceuticals in solid matrices found in the environment (e.g., manure, soil and sediment). In addition, it provides a general review of the occurrence and the fate of human and animal pharmaceuticals in the environment.

2. Pharmaceutical usage and classification

Representative human and animal pharmaceutical compounds used for therapeutic and non-therapeutic purposes are summarized in Table 1, including the estimated annual usage amount. According to Mellon et al. [4] in January 2001, human, agricultural, and companion animal antimicrobial usage now totals over 35 million pounds annually in the USA. Of the total usage, 14% is used for human and animal therapeutic purposes and 70% of antimicrobials are used in animals for non-therapeutic purpose, mainly as growth promoters. Thus, a major concern is the antimicrobials that are used in animals for non-therapeutic purposes.

Human pharmaceuticals found in the aquatic environment, mainly from sewage treatment plants (STPs), were classified in nine categories (analgesics, anti-inflammatory, antibiotics, antiepileptics drugs, β-blockers, blood lipid regulators, contrast media, cytostatic drugs, and oral contraceptives) depending on their use [9]. This study also points out that incomplete elimination of active pharmaceuticals in STPs causes most of the contamination in surface water.

Animal pharmaceuticals can be classified as therapeutic, used for treating illness or to prevent illness, or non-therapeutic, used primarily for enhancing the animals' growth, increasing the value of the animals with lower cost and in less time [10]. Depending on the different groups of animals, the same compound can be used for different purposes. For example, monensin, an ionophore polyether antimicrobial, is used in poultry for preventing *coccidiostats* and at the same time used as a growth promoter in beef and dairy cattle [11].

3. Analytical methods

3.1. Sample preparation and extraction

Methods of sample preparation and extraction for pharmaceuticals have evolved significantly for both aqueous and solid phases since they were first described as early as the late 1980s. The traditional sample-

Table 1. Summary of human and animal pharmaceuticals [4,9–11,41]

Subject	Use	Treatment details	Examples	Estimated annual used amount (thousand pounds)
Human	Therapeutic	Treatment of human diseases	*Analgesics and anti-inflammatory drugs*: acetaminophen, acetylsalicylic acid, diclofenac, ibuprofen, aminophenazone, codeine *Antibiotics*: clarithromycin, erythromycin, roxythromycin, lincomycin, sulfamethoxazol, ciprofloxacin, norfloxacin, tetracycline, oxytetracycline *β-Blockers*: metoprolol, propanolol, betaxolol, bisprolol, nadolol *Lipid-regulators*: bezafibrate, clofibric acid, fenofibrate, gemfibrozil *X-ray contrast media*: iopamidal, iopromide, iomeprol	3000
	Non-therapeutic	Other human use	Topical creams, soaps, disinfectants	1500
Animal	Antimicrobials	Treatment and prevention of bacterial diseases	Amoxicillin, chlortetracycline, dihydrostreptomycin, enrofloxacin, erythromycin, licomycin, oxytetracycline, sulfadiazine, tetracycline, tylosin	2000
	Coccidiostats and antiprotozoals	Prevention of coccidiosis and swine dysentery	Amprolium, clopidol, dimetridazole, lasalocid, maduramycin, narasin, nicarbazin	
	Growth promoters	Increase food digestion	Flavophospolipol, monensin, salinomycin	27,578
	Aquaculture treatment	Treatment of sea lice infestations and funrunculosis	Amoxicillin, azamethiphos, cypermethrin, emamectin, florfenicol, hydrogen peroxide, oxolinic acid, oxytetracycline	