Chemosphere 115 (2014) 81–87

Contents lists available at ScienceDirect

Chemosphere

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

Food safety/food security aspects related to the environmental release of pharmaceuticals

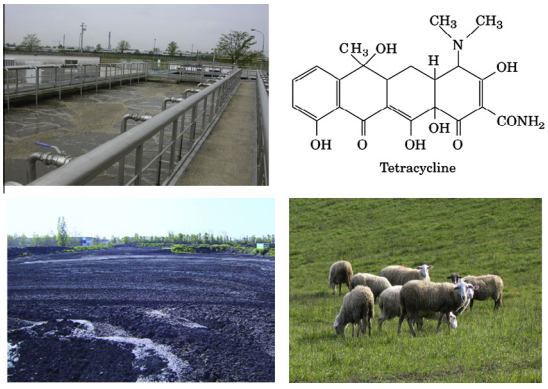
Gianfranco Brambilla [a,*], Cecilia Testa [b]

[a] Istituto Superiore di Sanità, Toxicological Chemistry Unit, Rome, Italy
[b] Istituto Zooprofilattico Sperimentale della Sardegna, Lab Drug Residues, Sassari, Italy

HIGHLIGHTS

- Top soil and surface water intake expose grazing animals to contaminants.
- Pharmaceuticals in the environment may be a risk for food safety/security.
- Proposed EQS in surface waters also seem appropriate for food safety assessment.
- The use of biosolids on pasture may represent a risk in free-grazing species.
- The definition of EQS in soil to support food safety and food security is envisaged.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 11 December 2013
Received in revised form 22 January 2014
Accepted 22 January 2014
Available online 3 March 2014

Handling Editor: J. de Boer

Keywords:
Pharmaceuticals
Top soil
Surface waters
Animal production
Food safety
Food security

ABSTRACT

The environmental presence of pharmaceuticals in top soil and in water where extensive animal farming occurs may represent an involuntary source of residues in food that might affect both food safety and food security. We modelled the presence of residues in animal matrices from the inventoried environmental concentration of selected drugs in surface waters (range: 0.1–10 μg L^{-1}) and agriculture soils (range: 1–100 μg kg^{-1} dry weight), accounting for animal production parameters (i.e., forages, water intake and milk and egg production) and drug pharmacokinetics. The results indicate that the contamination of tetracyclines in top soil may represent a major issue both for the compliance with maximum residue levels in food (100–300 ng g^{-1}) and for the claim of organic products. via surface water, animals may be vulnerable to the intake of anabolics and growth-promoting agents, such as 17-beta estradiol and clenbuterol, only under a worst-case scenario. Their identification, which is currently achievable at a pg g^{-1} level in animal specimens, is considered proof of illegal treatment and can lead to the prosecution of farmers. The Environmental Quality Standards that have been proposed for priority substances in surface waters may also be considered protective in terms of food security/food safety; however, a broad-spectrum characterisation of drugs within the agriculture context could be envisaged to refine the uncertainties in the risk assessment and for combined intakes.

1. Introduction

There is consolidated evidence that intensive farming systems (fattening calves, pigs, poultry, and aquaculture) represent a source

* Corresponding author. Address: Istituto Superiore di Sanità, Toxicological Chemistry Unit, Viale Regina Elena, 299, I-00161 Rome, Italy. Tel.: +39 6 4990 2764; fax: +39 6 4990 2836.
E-mail addresses: gianfranco.brambilla@iss.it (G. Brambilla), cecilia.testa@izs-sardegna.it (C. Testa).

http://dx.doi.org/10.1016/j.chemosphere.2014.01.024
0045-6535/

Nomenclature

BATs	Best Available Techniques
bw	body weight
COR	carry-over rate
d	day
dm	dry matter
E2	17 beta estradiol
EE2	ethinyl estradiol
EFSA	European Food Safety Authority
EMA (EMEA)	European Medicine Agency
EMAS	Eco Management and Audit Scheme
EQS	Environmental Quality Standard
EU	European Union
LC–MS/MS	liquid chromatography–tandem mass spectrometry
LoD	limit of determination
MoSS	margin of food safety/security
MRL	maximum residue limit
WWTP	waste water treatment plant

for the release of pharmaceuticals in the environment (Jjemba, 2002). Thus far, drugs with antimicrobial/anti-parasitic activity are the most practicable tools to limit the onset and spread of infectious diseases to high-density feedlots (EU Commission, 2010). Antimicrobials in medicated feeds and, to a lesser extent, in feed additive at doses up to g kg^{-1} in feed, as in the case of sulphonamides and tetracyclines, determine the presence of drug residues at the mg kg^{-1} level in animal dejects. Manure and slurry are then dressed on agricultural soils as fertilisers (Migliore et al., 2003, 2010); thus, determining the environmental release is also extended to endogenous hormones from pig breeding farms (Pinheiro et al., 2013). In the case of off-shore aquaculture farms, veterinary drugs and their metabolites are released directly into water bodies (Cabello, 2006). Therefore, registered veterinary drugs and additives should comply with an Environmental Risk Assessment during the authorisation procedure, and possible adverse effects on biota should be reported under pharmacovigilance programmes underpinned in the EU Commission Directive 2001/82/EC. Moreover, intensive animal farming settlements could apply to a voluntary *Eco-Management and Audit Scheme* (*EMAS*) (EU Commission Decision, 2011), i.e., through the application of the Best Available Techniques (BATs) (EU Commission, 2013), to mitigate the environmental impact of their activities.

In recent years, the evidence regarding the impact of the environmental quality on food-producing animals and their products in rural and extensive farming systems has progressively arisen. Priority contaminants, such as heavy metals and persistent organic pollutants, may affect the compliance with the food safety legislation of products from grazing cattle and pigs (Edwards, 2003; Gummow et al., 2006; Smith et al., 2009), free range flocks, (Van Overmeire et al., 2009), and extensively farmed fish (Miniero et al., 2013). In such cases, the animals' intake of contaminants that are associated with natural resources (top soil and the related fauna), grass, surface water and associated sediments, and air deposition on fodders may result in greater relevance than that associated with commercial feeds.

In this paper, we attempt to assess possible environmental quality parameters for the presence of pharmaceuticals in the agriculture zones that are devoted to extensive farming systems, both in terms of food safety (levels of authorised drugs in veterinary medicine below the maximum residue limit in edible tissues) and food security (presence of unauthorised/undeclared drugs below their analytical thresholds), as far as the involuntary presence of food residues of an undeclared/unauthorised drug may severely affect the socio-economics of the farming system, according to the food safety legislation in place within the European Union. Within the sustainability policies to reduce the carbon- and water-footprints in food production systems, the proposed use of bio-solids as top soil enhancers in agriculture (Chen et al., 2012) and the watering of fodders from reclaimed waters (Arnold et al., 2012), which both originate from urban waste water treatments plants, as well as the direct animal intake of pharmaceuticals from freshwater, may represent an emerging source of xenobiotics into the food chain.

2. Materials and methods

2.1. Pharmaceuticals in top soil and surface water are of relevance for food safety/food security

The group of tetracyclines (oxy-, chlor-, tetra-, doxycycline) have been considered because these drugs are among the most prescribed antimicrobials in both veterinary and human medicine and because of their ability to bind humic acids and metals that are present in top soil (Hamscher et al., 2002; Blackwell et al., 2009). Their concentration ranges in agricultural soils have been derived from the international literature, which was reviewed by the Bio Intelligence Service (2013). Because of their wide consumption in both human and veterinary medicine and because of their relevance in pharmacoresistance outbreaks, along with their ability to bind to soil, fluoroquinolones were also accounted for (Leal et al., 2013). For surface waters, the group of sulphonamides, as drugs that are more prone to be released in WWTP effluents, have been chosen according to Loos et al., 2008. Moreover, the concentration of anti-asthmatic drugs, such as albuterol/salbutamol and clenbuterol, have also been considered due to their proposition in the recent past as growth promoting agents in feedlots; their use is currently forbidden in the European Union and is severely prosecuted and fined (EU Directive 96/23/EC, Annex I). Under this perspective, estrogens, such as ethinyl estradiol (EES) and 17 beta estradiol (E2), which are either listed in the above quoted Annex A or next to be framed within the European Parliament Directive 2013/39/EC as priority substances for their potential harmful effects in the aquatic environment, have also been accounted for. Our attention has also been focused on diclofenac, which is a non-steroidal anti-inflammatory drug licensed in veterinary medicine (EMA, 2009) but of potential eco-toxicological concern in water bodies (Johnson et al., 2013). Other pharmaceuticals, such as thiabendazole, which is an anti-parasitic and anti-fungal drug that is commonly used in animals and in agriculture (Correa and Escandar, 2006), and lorazepam, which is a short-acting benzodiazepine from human prescriptions (Mendoza et al., 2013), have been included in this assessment because of the reported concentrations above 1 μg L^{-1} in surface waters, which may represent a potential risk in animal food production systems. The amounts, which refer to the sales, of the main classes of antimicrobials that are prescribed in veterinary medicine and that are considered environmental contaminants in top soil and surface water are reported in Fig. 1.

2.2. Top soil intake in grazing animals

Several papers examine top soil intake in farmed animals, with reported differences among species and seasonal variations