

Assessment and Management of Pharmaceutical Substances in the Environment

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Abstract. The occurrence of pharmaceutical substances and its migration in aquatic ecosystems has recently raised a serious public concern as well as relevant environmental issues all over the world. The main objective of the research was to perform the flow analysis of the investigated substances and to provide recommendations on how to reduce pollution of the selected pharmaceuticals in Lithuania.

Keywords: Pharmaceuticals · Pollution · Environmental risk assessment · Sustainability · Management

1 Introduction

The 2030 Agenda for Sustainable Development, adopted by all United Nations Member States in 2015, provides a shared blueprint for peace and prosperity for people and the planet, now and into the future. The ambitious aims by 2030, substantially reduce the number of deaths and illnesses from hazardous chemicals and air, water and soil pollution and contamination [1]. In its communication introducing The European Green Deal (EGD) [2], the European Commission stressed the importance of transforming the EU's economy to a sustainable future, and to mainstream sustainability in all EU policies, linking it also to the United Nation's 2030 Agenda and the Sustainable Development Goals (SDGs). While an unprecedented worldwide effort is under way to fight the COVID-19 pandemic, the persistent threats to the health of our planet call for urgent remedies too [3].

In 2018, 5th of June decision of European Commission established a *Watch list* of substances for Union-wide monitoring in the field of water policy [4]. This list was for supporting future prioritization exercises was established in all EU countries. Pharmaceutical substances, such as *antibiotics - erythromycin, azithromycin and clarithromycin* were included in this list, in order to gather Union-wide monitoring data for facilitating the determination of appropriate measures to address the risk posed by those substances. As for water and soil pollution from pharmaceuticals, in addition to the EU target on antimicrobial sale reduction, the Commission will encourage international cooperation to address the environmental risks in other countries where pharmaceutical emissions

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from manufacturing and other sources may contribute, among other things, to the spread of antimicrobial resistance (AMR) [3].

Article 8c of the Priority Substances Directive (2008/105/EC1 as amended by Directive 2013/39/EU2) requires the European Commission to propose a strategic approach to the pollution of water by pharmaceutical substances. With the present Communication, the Commission is delivering on that legal obligation, as well as on a call referred to in the pharmacovigilance legislation to examine the scale of the problem of pollution of water and soils with pharmaceutical residues [6]. In particular to achieving SDG 6 on clean water and sanitation.

The overall quality of water in Lithuania's rivers has improved significantly over the past decade thanks to large investments in wastewater management system. However, the Curonian Lagoon, the Baltic Sea shore, about two-thirds of Lithuania's rivers and about one-third of lakes do not meet yet the requirements for a good status of water (share of water bodies of good water status accounted for 54%). The occurrence of pharmaceutical substances and its migration in aquatic ecosystems has recently raised a serious public concern as well as relevant environmental issues not only all over the world, but in Lithuania as well.

A holistic approach taking into consideration the sources of these substances, discharges and related risks for the environment, it is therefore essential to anticipate and manage those compounds in the environment. Until today, no many investigations were made regarding these pharmaceutical substances investigations in Lithuania. Therefore, made research is important for both the actual substances identification in the aquatic environment and the management with the aim to reduce the toxicological risk posed to the environment and human health.

2 Sources and Pathways

Pharmaceuticals are a widely recognized, effective treatment for many human and animal diseases. The 2019 EU Strategy on Medicinal Products for the Environment states that the EU currently allows about 3,000 active pharmaceutical ingredients. The availability of medicines for human and veterinary use has doubled in 6 years (2005–2014) [7]. The EU sells about 25% of medicines to humans and 31% to veterinary medicine. With the increase in the consumption of pharmaceutical active substances in society, the problem of increased pollution is observed. There is growing evidence of the release of active substances into the environment. Even low concentrations of pharmaceuticals can be toxic to humans and ecosystems.

Various pharmaceuticals, such as antibiotic residues, enter the aquatic and terrestrial environment through a variety of routes, such as municipal wastewater discharged from urban treatment plants. Due to the composition and properties of antibiotics, up to 90% of pharmaceutical residues enter the environment in their original form [7]. In this way, some pharmaceutical substances end up due to improper disposal of unused medicines (discharges into sinks or toilets). Another way is by spreading animal manure. It is one of the untreated sources of livestock pollutants. Pharmaceutical substances also reach the environment in other ways: directly from with industrial effluents, through treated or untreated wastewater discharged and sewage sludge, from veterinary services for pets

and from improper disposal of drug-contaminated waste in landfills, animal feed and aquaculture ponds (Fig. 1) [8].

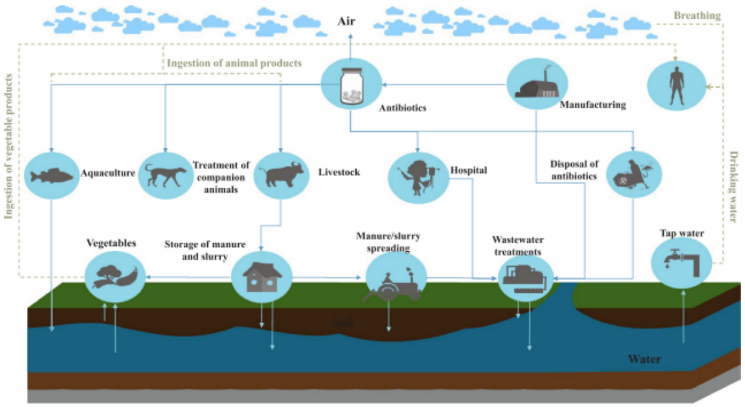

Fig. 1. Human exposure to antibiotic resistance associated with antibiotic residues in the environment [8]

Of all the other antibiotics in use in the world, the *macrolide antibiotics* are *erythromincin, clarithromycin and azithromycin.* The organic composition does not allow them to degrade naturally, so these antibiotics are also included in the group of persistent contaminants [9]. According to the Eurobarometer 478 survey published by the EC, about 31% of the Lithuanian population in 2017 used antibiotics in the form of tablets, powder or treacle. As many as 92% of respondents received antibiotics from a health care professionals. While 27% had a prescription, 65% received antibiotics directly from a doctor, 4% of respondents used available antibiotic residues, and as many as 3% purchased over-the-counter medications [10] (Table 1).

Table 1. Consumption of research materials in Lithuania in 2015–2018

Researched substance	Year	DDD/1000 inhabitant/per day
Erythromycin	2015	0,0167
	2016	0,0144
	2017	0,0114
	2018	0,0103
Clarithromycin	2015	1,42
	2016	1,55
	2017	1,63

(*continued*)

Table 1. (*continued*)

Researched substance	Year	DDD/1000 inhabitant/per day
	2018	1,68
Azithromycin	2015	0,506
	2016	0,433
	2017	0,470
	2018	0,459

3 Management of the Risks

According the results of the substance flow analyses (SFA) the highest consumption of pharmaceuticals occurs in households, where it is quite difficult to control wastewater (Table 2).

Table 2. Quantities of pharmaceutical substances in effluents in 2017 [11]

Pharmaceuticals	Concentrations before treatment, ng/l/Concentrations after treatment, ng/l				
	City 1	City 2	City 3	City 4	
Azithromycin	37,0/13,4	76,4/19,9	182,4/12,1	11,9/11,0	2017
Clarithromycin	126,5/229,3	474,8/150,2	1326,7/73,7	243,6/62,0	
Erythromycin	95,5/75,2	49,9/29,3	359,2/33,0	2,5/3,9	

A possible solution would be to separate domestic effluent streams from other streams in order to allow for analysis that is more extensive and monitoring in the environment to assess which streams generate the highest pollutant loads after domestic effluents. It would be possible to monitor individual flows more actively and to find new solutions to control them. For example, separating flows from hospitals and the outpatient sector could treat wastewater before handing it over to urban wastewater treatment plants (WWTPs). Assessing the efficiency of wastewater facilities could also lead to more efficient and easy-to-implement solutions for further treatment.

The scientific literature indicates that 50% to 67% of erythromycin is excreted in the environment with wastewater, with other antibiotics entering the environment in an amount of 30% to 90%, depending on their chemical composition [12, 13]. Because macrolide antibiotics have similar chemical composition and properties, it is estimated that approximately 60% of erythromycin, clarithromycin, and azithromycin enter the environment through the effluent.

The effects of the pharmaceutical substances on human health and the natural environment are not widely known. Monitoring of pharmaceuticals is limited and requires more accurate analytical solutions and methods. More information on the effects and

concentrations of relevant substances in the aquatic environment could lead to more research.

It is important to educate the population and medical staff about the proper use of medicines, the consequences of improper unused pharmaceuticals disposal. It would be possible to draw the attention of the population to informative surveys about the risks of pharmaceuticals to the environment and their use. Encourage citizens to use antibiotics responsibly, to buy only prescription medicines from reliable sources, to stop using obsolete and unsuitable medicines, and not to share medicines with relatives or engage in self-medication. The government should organise the campaign to inform the public about the correct disposal of pharmaceuticals by delivering them to the pharmacy and about unauthorized disposal methods such as disposal in containers or disposal directly into sewer.

It is likely that new legal requirements regarding the generation of wastewater polluted by pharmaceutical substances will come very soon in country, as there are many different initiatives regarding the micropollutants, as well pharmaceuticals, in the waster cycles. A lot of attention should be paid to the qualitative parameters at the points of discharge wastewater to the sewage systems as well to the natural environment, as well use of the pharmaceuticals and discharge from the health care institutions.

Particular attention must be paid to informing consumers about not only the benefits of antibiotics, but also the damage they cause to the environment and to humans.

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