Studii şi Cercetări	Martie 2023	Biologie	32/1	108-113	Universitatea"Vasile Alecsandri" din Bacău

AN OVERVIEW OF PHARMACEUTICAL POLLUTANTS IN THE ENVIRONMENT

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Key words: *pharmaceuticals, pollution, environment*

INTRODUCTION

Pharmaceuticals and their derivatives have become a matter of concern nowadays (Acs et al., 2022), both for human health and the environment. The effects of such compounds commonly detected in water environments remain largely unknown, but research is beginning to gain ground.

This is a consequence of the excessive use of drugs globally, on the one hand, and, on the other hand, insufficient or inadequate wastewater treatment (Ortuzar et al., 2022), with many treatment plants being unable to remove completely these residues, due to the lack of technology. Even in very small amounts, these pharmaceutical residues, often present in the form of hard-to-detect nanoparticles, can have negative effects on the population (Desai et al., 2022).

These insufficiently treated waters before being discharged into the natural environment (rivers, lakes) lead to ambient exposure to active pharmaceutical ingredients, which can have negative effects on the health of aquatic ecosystems (Hong et al., 2021), as well as on humans (Wilkinson et al., 2022).

There is, however, a possibility of reprocessing these waters if introduced into the drinking water system, if treatments do not completely remove some active pharmaceuticals. Therefore, recent research is based on the removal of these pollutants by various methods (e.g. biological, chemical) and technologies (UV treatment, active charcoaltreatment) (Onesios-Barry et al., 2014). The ingredients of pharmaceutical nature most commonly detected in these waste waters were antiepileptics, antidiabetics, anti-inflammatory and antibiotic substances.

Several studies have reported the presence of phenytoin (antiepileptic) in sewage treatment plant effluents, hospital effluents, surface water and even drinking water (Cardoso-Vera et al., 2022).

Solutions to combat water contamination with pharmaceutical pollutants would be long lasting. This means putting in place the necessary infrastructure to capture and treat wastewater, i.e. that treatment plants use new technologies to completely stop active pharmaceutical substances.

An immediate solution, on the other hand, could be the proper use of medicines, namely through a more difficult release of antibiotics and stricter dose restrictions.

The aim of this article is to have an overview on the current concentrations found in the environment worldwide so far.

POLLUTION BY ACTIVE PHARMACEUTICAL SUBSTANCES

An active pharmaceutical compound is a substance used in the development process of a medicinal product, and through use in the manufacturing process, becomes an active ingredient of that product, which is intended to manifest a pharmacological, immunological or metabolic action in order to restore, correct or modify physiological functions, or is intended to establish a medical diagnosis.

Nowadays, pharmaceutical pollution is an issue of great concern worldwide (Wohler et al., 2020), both through active pharmaceutical ingredients and inert substances also (such as packaging), which have created considerable interest (Desai, et al 2022) and can have negative effects on the environment and humans (Wilkinson et al., 2022; Millarhouse et al., 2020).

These pollutants can have harmful effects even in very small quantities (Desai et al., 2022). Therefore, recent research has focused on the disposal of these waste pharmaceuticals (Onesios-Barry et al., 2014).

Currently, residual pharmaceuticals have started to be monitored because they have been detected in effluents and surface waters (Quesada et al., 2019).

Another current issueis that some of the active pharmaceutical ingredients are not completely removed by wastewater treatment processes (Klimaszyk and Rzymski, 2018).

SOURCES OF PHARMACEUTICAL POLLUTANTS

There are numerous sources of pharmaceutical pollutants, and these can be generated from:

a) Human excretion: Human bodies digest and excrete pharmaceutical drugs after they ingest them.

Then, through urine and faeces, these drugs can end up in wastewater systems (Lienert et al., 2007).

b) Improper disposal of unwanted or expired medicines, such as flushing them down the toilet or in the rubbish (Rogowska and Zimmermann, 2022).

c) Agriculture: Antibiotics and other drugs used in livestock production can be disposed of into the environment through animal faeces and water runoff (Manyi-Loh et al., 2018).

d) Pharmaceutical manufacturing: Production facilities have the potential to accidentally release pharmaceutical chemicals and by-products into the environment (Larsson, 2014).

The presence of these substances in the environment is due to consumers, through the use and disposal of medicines. Only a small percentage of administered drugs are metabolised; the rest can be eliminated through sweat, but most are expelled from the body through urine or faeces, which means that they will end up in wastewater and eventually in the environment. The use for irrigation of insufficiently treated wastewater, as well as a lack of waste management and treatment infrastructure, leads to increasing pharmaceutical contamination as well as pathogen impacts on human and animal health (Singh, 2021).

For instance, the impact of clinically relevant antimicrobial resistance genes and antibiotic-resistant bacteria released from anthropogenic sources, combined with their overuse in human or veterinary medicine and agriculture, is currently considered an environmental problem (Crettels et al., 2023) which may also impact on human health (Dong et al., 2023).

A recent study (Wilkinson et al., 2022) shows that at at least 25.7% of sites where water samples were analyzed, concentrations of at least one active pharmaceutical substance exceeded the limits of concentrations considered safe for aquatic organisms.

This poses risks to aquatic ecosystems (Zheng et al., 2022), but also to humans due to antibiotic resistance (Wilkinson et al., 2022).

ENVIRONMENTAL EFFECTS OF PHARMACEUTICAL POLLUTANTS

Pharmaceuticals residues in the environment have the potential to impact both terrestrial and aquatic ecosystems (rivers, lakes, groundwater and seas). These substances have the potential to interfere with the endocrine systems of aquatic organisms, which could affect their reproductive and developmental capabilities.

Some drugs can persist in the environment for long periods of time and possibly causing bioaccumulation in the food chain.

The combination of low cost and over-the-counter sales of some medicines has greatly increased concerns about their disposal into the environment.Pharmaceutical substances have been disposed off in the environment for decades, but the concern of researchers has only recently become visible (Boxall, 2004).

Pollution with pharmaceuticals can have effects on biocenosis. For instance, in natural waters there may be long-term effects on the behaviour or reproduction of aquatic species (Doerr-MacEwen and Haight, 2005). Another problem for fish, can be related to migration and disruptions to the balance between providing resources and minimising the risk (Poiverino et al., 2021).

Astudy performed by Carter et al., 2016 demonstrated that the internal pH of *Eisenia fetida* is altered due to incubation in soil enhanced with pharmaceuticals. Thus, it is concretized that these pharmaceuticals can modify both the soil chemistry and the earthworms metabolism.

Therefore, the ecological risks that these drugs may present cannot be excluded.

Some studies have reported that valproic acid was detected in tributaries samples analysed: 130 ng $L^{-1}$from Back River sewage systems, USA (Yu et al., 2012), respectively 140 ng L^{-1} of from the waste treatment plant Baltimore, MD (Yu et al., 2006). In both cases, measurement swere also made in effluent waters. In Table 1 the amounts of pharmaceutical pollutants found in the environment in different parts of the world have been summarised.

Table 1. Concentrations of pharmaceutical pollutants found in different matrices

	Pharmaceutical Substance	Sample collecting	Concentrations	References
Antibiotics	**Meropenem**	Raw samples from the wastewater treatment plants	Before treatment 15 ng L^{-1} After treatment 10 ng L^{-1}	(Tran et al., 2016)
	Meropenem	Effluent from a treated wastewater based on mixture of clinical and urban wastewater total quantity 17.5 million m^3/a	0.2 μg L^{-1}	(Voigt et al., 2020)
		Total clinical waste waters from a clinical-urban system of a maximum care hospital	197 μg L^{-1}	

	Meropenem	Hospitals	0.19 µg L^{-1} 1.01 µg L^{-1}	(Thai-Hoang et al., 2016)
		Mixed manhole hospital	1.07 µg L^{-1}	
	Imipenem	Hospital effluent wastewater	14.42 µg L^{-1} hospital effluent	(Szekeres et al., 2017)
	Ceftazidime	Clinical-urban wastewater system	Influent 11.7 µg L^{-1}	(Voigt et al., 2020)
Antidepressants	**Fluoxetine**	Rivers in Madrid, Metropolitan Area	Min. 8 ng L^{-1} Max. 44 ng L^{-1} Average 14 ng L^{-1} from all points collected	(Alonso et al., 2010)
Antiepileptics	**Valproic acid**	Back River Wastewater Treatment Plant - influent and effluent	Influent 130 ng L^{-1} Effluent ND	(Yu et al., 2012)
	Valproic acid	RWWTP, Baltimore, MD	Influent 140 ng L^{-1} Effluent ND	(Yu et al., 2006)
	Valproic acid	Influent	1006 ng L^{-1}	(Borova et al., 2014)
		Effluent	232.8 ng L^{-1}	
		Influent	3008 ng L^{-1}	
		Effluent	264.3 ng L^{-1}	
		Influent	1571 ng L^{-1}	
		Effluent	321.6 ng L^{-1}	
		Influent	366.4 ng L^{-1}	
		Effluent	202.8 ng L^{-1}	
		Influent	916.1 ng L^{-1}	
		Effluent	790.3 ng L^{-1}	
	Ibuprofen	Waste waters	45 µg L^{-1} 703-1673µg L^{-1} 1.38 µg L^{-1} 5.78 µg L^{-1}0.98 µg L^{-1}	(Chopra and Kumar, 2020)
		Surface waters	1-67 µg L^{-1} <14-414 µg L^{-1} 5-280 µg L^{-1} 8 µg L^{-1} 1417 µg L^{-1}	
	Ibuprofen	Lima River	723 ng L^{-1}	(Paiga et al., 2013)
		Hospital effluent	3,868 ng L^{-1}	
		Landfill (Leachate)	48,720 ng L^{-1}	
		Wastewater treatment plant (WWTP) effluent	616 ng L^{-1}	
		WWTP (Algeria)	0.34-0.43 µg L^{-1}	
		Algiers WWTP (Algeria) Drinking water	0.31 µg L^{-1}	
		Algiers WWTP (Algeria) Surface water	0.37 µg L^{-1}	

Anti-inflammatories	**Ibuprofen**	Nairobi River Basin (Kenya)	30 μg L^{-1}	
		Egypt, Assiut	6.7 μg L^{-1}	
		Lake Victoria, Uganda	0.78 μg L^{-1}	
		Umgeni River	12.94 μg L^{-1}	
		Umgeni River	84.6 μg L^{-1}	(Waleng and Nomngongo, 2022)
		S and N of Durban city	3.87-67.9 μg L^{-1}	
		Msunduzi River	85 μg L^{-1}	
		Nigeria, Ogun State	3.04 μg L^{-1}	
		Nigeria, Lagos, Oyo and Orgun States	ND-2.1 μg L^{-1}	
		Nigeria, City of Lagos	<0.004-2.74 μg L^{-1}	
		Nigeria, Lagos, Oyo and Orgun States	<0.002-8.84 μg L^{-1}	
		Singapore WRP	0.87-1.07 μg L^{-1}	
	Ketoprofen	Catalonia (Spain) in rivers and effluents	0.87 μg L^{-1} 0.3 μg L^{-1}	(Farre et al., 2001)

CONCLUSIONS

Research on pharmaceutical pollution will contribute significantly to the understanding of the impact of medicines on ecosystems and will bring important benefits for environmental conservation as well as for public health.

ABSTRACT

Pharmaceutical pollution is a new area that has attracted interest because of its environmental detrimental effects. A major issue currently is the usage that leads to abuse, which leads to the further release of chemicals into the environment.

A very wide range of pharmaceutical substances, from anti-epileptics, anti-inflammatories, antibiotics, antidepressants or anti-diabetics, are present in the environment. These substances have been frequently detected in recent years from waste water, surface water, groundwater and even in drinking water.

This has raised public health concerns and therefore further research studies are needed to fill the information gaps in this field.

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