

WATER REUSE MANAGEMENT

IS PHARMACEUTICAL
POLLUTION A REAL PROBLEM?



INTRODUCTION

Water scarcity and droughts currently affect many European regions.¹ Statistics show that by 2007, at least 11% of European citizens and 17% of Europe's territory had been affected by a scarcity in water supply. It is estimated that droughts in Europe over the past thirty years have incurred costs of up to €100 billion. This situation is expected to worsen due to climate change but water reuse could pose a possible solution, if properly explored.^{1,2}

Water reuse refers to the use of treated wastewater to increase the available water supply in communities while ensuring high quality, especially in times of drought.

In 2012, the European Commission (EC) announced its intention to tackle the issue of water scarcity and reuse, and supported the need for increasing water reuse in its Communication, A Blueprint to Safeguard Europe's Water Resources.³

At present, the EC is working to develop minimum quality requirements for water reuse in the EU, taking into consideration the fate of emerging contaminants* after irrigation with reclaimed wastewater.⁴ Pharmaceuticals are among the long list of emerging contaminants that show persistence and can bioaccumulate in different environmental compartments. Their presence in treated wastewater should therefore be accurately addressed.

* Emerging contaminants include substances that are persistent, bioaccumulative, and toxic (PBTs), persistent, mobile and toxic (PMTs), very persistent and very bioaccumulative, as well as substances affecting endocrine-related functions. These chemicals are not commonly monitored in the environment, but can enter the environment and cause predictable or unpredictable side effects to both human health and the environment.



WASTEWATER TREATMENT EFFLUENTS ARE PARTICULARLY PROBLEMATIC

The presence of emerging contaminants, particularly pharmaceuticals, in effluent from wastewater treatment plants (WWTPs) has been extensively described in the recent scientific publications.^{5,6,7}

Current wastewater treatment methods can only partially remove pharmaceuticals, meaning residues are still present in effluent. Examples of residues detected in effluent include:

- Lipid regulators, anti-inflammatories, and antibiotics, which have been found in influents and effluents of WWTPs in Portugal.⁸
- Anti-inflammatories such as ibuprofen and diclofenac, the antibiotics erythromycin and oxytetracycline, and the female sex hormone 17b-estradiol have all been found in the final effluent of WWTPs in the UK.⁹

In both cases, the concentrations of these drugs were high enough to potentially cause harm to ecosystems.

Even low concentrations of pharmaceuticals have harmful effects on animal and plant life. Some of the effects of pharmaceuticals in the environment described in research are:

- Residues of diclofenac, an anti-inflammatory drug, can cause renal failure in vulture populations feeding on carcasses of cattle treated with the drug. As a consequence the vulture population in the Indian subcontinent declined by 80-99% between 2003-2004¹⁰
- The contraceptive drug ethinylestradiol can impair reproduction in fish population¹¹
- The antibiotics enrofloxacin and ciprofloxacin have toxic effects and can inhibit the growth of aquatic species such as cyanobacterium and duckweed¹²



Disinfection processes at WWTPs cannot completely inactivate local microorganisms, which are able to re-grow post treatment when they find favourable conditions.^{13,14,15}

In addition, very little is known about the fate of antibiotic resistant bacteria and antibiotic resistance genes in soil after irrigation with wastewater. Scientific evidence suggests that some antibiotic resistant bacteria can proliferate in soil or plants, behaving as an invasive species and some antibiotic resistance genes can be transferred** from wastewater bacteria to soil or plant bacteria.¹⁶

WHAT FACTORS DETERMINE THE EFFICIENCY OF REMOVING PHARMACEUTICALS FROM WASTEWATER?

1. **The chemical composition profile of a pharmaceutical** – for example, the size of the molecule, the chemical structure of both the active pharmaceutical substance, and the excipients (i.e. the substances with no medicinal effects which are also added to pharmaceuticals)
2. **The specific wastewater treatment process applied**
3. **The initial concentration of pharmaceuticals in the influent⁴** - for example, the influent from hospitals has high concentrations of pharmaceuticals, so their removal at WWTPs can be very challenging

To give just one example of the difference in efficacy of pharmaceutical removal - after wastewater treatment ibuprofen has a removal rate of >90%, while carbamazepine has a rate of <10%.¹⁷

** This is achieved through a mechanism called horizontal gene transfer, which is the main mechanism for the spread of antibiotic resistance in bacteria.

THE ADDED PROBLEM OF TRANSFORMATION PRODUCTS

Some pharmaceuticals can have a high removal rate, but their transformation products*** are of particular concern. For example, metformin - the most commonly prescribed drug in the treatment of diabetes - can theoretically be removed with a potential >98% success rate in sewage treatment plants. During water treatment, however, metformin can be transformed to guanylurea, its transformation product. In this form, 82% of the metformin initially present in wastewater can be detected in effluent after treatment.¹⁸



*** Most pharmaceuticals undergo changes to their chemical structure before excretion, while passing through human or animal bodies, resulting in metabolites. After excretion, both active pharmaceutical ingredients and their metabolites will be present in the environment where they can further undergo changes to their chemical structures due to naturally occurring processes and technological processes (i.e. effluent treatment). These changes result in what are known as transformation products.

WASTEWATER TREATMENT TECHNOLOGIES ARE NOT YET ADVANCED ENOUGH TO DEAL WITH THE PROBLEM

Although some recent research has been conducted into wastewater treatment technologies and the factors that influence the removal of pharmaceuticals, innovation is needed in this field in order to minimise pharmaceuticals entering into the environment.

For example, one method of wastewater treatment used for drinking water that combines ozone and granular activated carbon was proved effective in removing most antibiotics.¹⁹ This treatment, however, is not as effective at removing other drugs, such as the antiviral drug acyclovir. The oxidation of acyclovir and its biotransformation product carboxy-acyclovir by ozone actually results in a stable but toxic transformation product called COFA.²⁰ COFA was shown to be toxic for *Vibrio fischeri* sp. - a bacteria that can be naturally found in seawater and fresh water.²⁰

PHARMACEUTICAL POLLUTION IN WASTEWATER AND SOIL

In order to provide the nutrients essential to support plant life, manure and sludge are added to soil during the so-called “amending process”. In areas with high water scarcity, irrigation in agriculture is achieved using reclaimed wastewater.⁴ This is particularly problematic, however, as sludge, manure, and wastewater have all been shown to contain a series of contaminants, including pharmaceuticals.²¹



Irrigation with reclaimed wastewater may result in high levels of pharmaceutical pollution, particularly from pharmaceuticals that have relatively high solubility in water.

In recent years, scientists have explored the accumulation of pharmaceuticals in plants growing in amended soil or soil irrigated with reclaimed wastewater; research has shown that plants accumulate pharmaceuticals from the media where they grow.^{4,21}

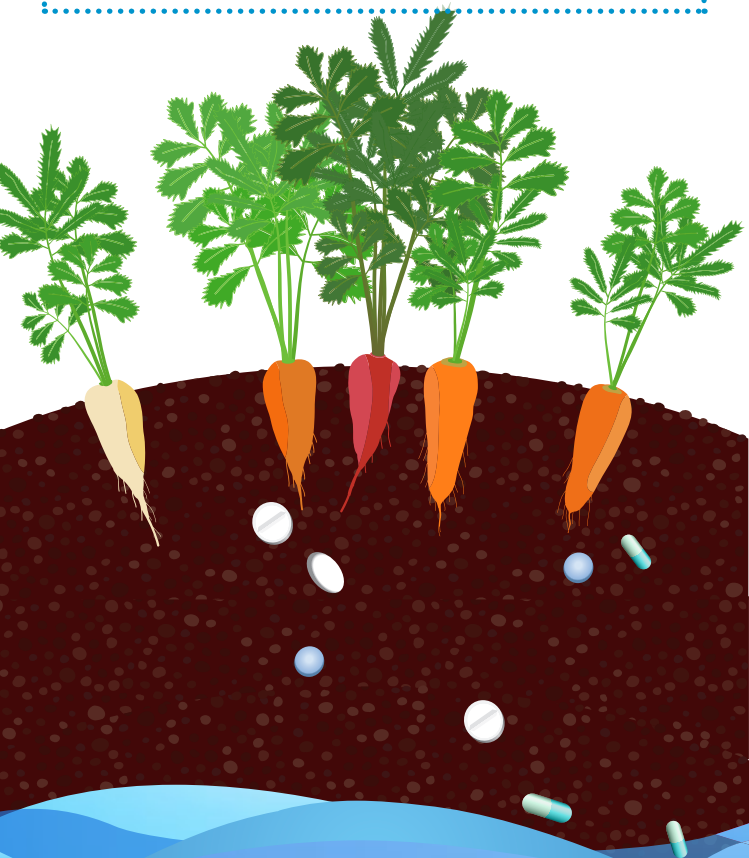
Crop plants grown on land that has been irrigated with reclaimed wastewater have higher levels of exposure to pharmaceuticals than those grown on land to which manure or sludge has been added.^{4,21}



PHARMACEUTICALS IN PLANTS

The veterinary medicines florfenicol, levamisole, and trimethoprim have been shown to accumulate in lettuce leaves, and enrofloxacin, florfenicol, and trimethoprim in the roots of carrots grown in contaminated soil. Scientists have concluded that measurable residues of these medicines are likely to occur in soils for at least five months following application of manure containing these compounds.²²

Furthermore, a research study investigated whether 20 frequently occurring pharmaceuticals could accumulate in four plants species (lettuce, spinach, cucumber, and peppers) grown in a nutrient solution containing low concentrations of the above pharmaceuticals. All pharmaceuticals were detected in the roots of the plants and 13 were also present in the leaves of the plants.²³



Furthermore, exposure during irrigation can take place during the entire life cycle of the plant, and the plants' capacity to accumulate pharmaceuticals from the soil increases over time. On the contrary, the exposure of plants to pharmaceuticals via manure or sludge decreases over time as plants naturally reduce their uptake of fertiliser.^{4,21}

How should pharmaceutical pollution in water reuse be addressed?

Water reuse can be beneficial in regions suffering from water scarcity, however, to ensure high water quality and protect human and environmental health, legislative measures should consider pharmaceutical pollution and the spread of antimicrobial resistance when proposing minimum quality requirements for water reuse.

RECOMMENDATIONS FOR EU POLICY MAKERS

- Establish quality standards/requirements to ensure that pharmaceuticals and antimicrobial resistant microorganisms in irrigation water, manure, and sewage sludge are controlled and limited in order to protect the environment
- Develop guidelines for EU Member States to carry out targeted monitoring of pharmaceuticals in water reuse
- Provide EU funding for innovative water treatment technologies that would reduce the level of pharmaceuticals in wastewater, including antibiotics and other antimicrobial resistant microorganisms

REFERENCES

1. SCHEER (2017). Scientific advice on Proposed EU minimum quality requirements for water reuse in agricultural irrigation and aquifer recharge. Available at: https://ec.europa.eu/health/sites/health/files/scientific_committees/scheer/docs/scheer_o_010.pdf
2. European Commission (2016). Water Scarcity & Droughts in the European Union. Available at: http://ec.europa.eu/environment/water/quantity/scarcity_en.htm
3. European Commission Communication COM(2012)673. A Blueprint to Safeguard Europe's Water Resources. Available at: <http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52012DC0673&from=en>
4. Deloitte (2017). Options for a strategic approach to pharmaceuticals in the environment. Available at: https://ec.europa.eu/info/sites/info/files/study_report_public_consultation_pharmaceuticals_environment.pdf
5. Ternes T., Joss A., and Oehlmann J. (2015). Occurrence, fate, removal and assessment of emerging contaminants in water in the water cycle (from wastewater to drinking water). *Water Research*, 72, pp.1–2. Available at: <https://www.sciencedirect.com/science/article/pii/S0043135415001360>
6. Evgenidou, E.N., Konstantinou I.K., and Lambropoulou D.A. (2015). Occurrence and removal of transformation products of PPCPs and illicit drugs in wastewaters: A review. *Science of The Total Environment*, 505, pp.905–926. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25461093>
7. Petrie B., Barden R., and Kasprzyk-Hordern B. (2015). A review on emerging contaminants in wastewaters and the environment: current knowledge, understudied areas and recommendations for future monitoring. *Water Research*, 72, pp.3–27. Available at: <https://www.sciencedirect.com/science/article/pii/S0043135414006307>
8. Pereira et al. (2015). Environmental impact of pharmaceuticals from Portuguese Wastewaters: geographical and seasonal occurrence, removal and risk assessment. *Environmental Research*, 136, pp.108–119. <https://www.ncbi.nlm.nih.gov/pubmed/25460627>
9. UK Water Industry Research (2014). Risk Based Prioritisation of Pharmaceuticals. Available at: <https://www.ukwir.org/reports/14-WW-17-16/115396/Risk-Based-Prioritisation-of-Pharmaceuticals>
10. Swan et al. (2006). Removing the Threat of Diclofenac to Critically Endangered Asian Vultures. *PLoS One*. Available at: <http://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.0040066>
11. Nash et al. (2004). Long-term exposure to environmental concentrations of the pharmaceutical ethynylestradiol causes reproductive failure in fish. *Environmental Health Perspectives*, 112(17), pp.1725–1733. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1253666/>
12. Ebert et al. (2011). Toxicity of the fluoroquinolone antibiotics enrofloxacin and ciprofloxacin to photoautotrophic aquatic organisms. *Environ Toxicology and Chemistry*. 30(12), pp.2786–92. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/21919043>
13. Li et al. (2013). Inactivation, reactivation and regrowth of indigenous bacteria in reclaimed water after chlorine disinfection of a municipal wastewater treatment plant. *Journal of Environmental Sciences*, 25, pp.1319–1325. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/24218842>
14. Fiorentino et al. (2015). Inactivation and regrowth of multidrug resistant bacteria in urban wastewater after disinfection by solar-driven and chlorination processes. *Journal of Photochemistry and Photobiology B: Biology*, 148, pp.43–50. Available at: <http://www.sciencedirect.com/science/article/pii/S1011134415001128>
15. Giannakis et al. (2016). Micropollutant degradation, bacterial inactivation and regrowth risk in wastewater effluents: Influence of the secondary (pre)treatment on the efficiency of Advanced Oxidation Processes. *Water Research*, 102, pp.505–515. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/27403873>
16. Becerra-Castro et al. (2015). Wastewater reuse in irrigation: A microbiological perspective on implications in soil fertility and human and environmental health. *Environment International*, 75, pp.117–135. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25461421>
17. Joss et al. (2005). Removal of pharmaceuticals and fragrances in biological wastewater treatment. *Water Research*, 39, pp.3139–3152. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/16043210>
18. Oosterhuis M., Sacher F., and Ter Laak T.L. (2013). Prediction of concentration levels of metformin and other high consumption pharmaceuticals in wastewater and regional surface water based on sales data. *Science of The Total Environment*, 442, pp.380–388. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/23183121>
19. Guillon et al. (2015). Study on veterinary and human antibiotics in raw and treated water from a French basin. *Water Science & Technology: Water Supply*, 15(6), pp.1275–1284. Available at: <http://ws.iwaponline.com/content/15/6/1275>
20. Prasse et al. (2012). Oxidation of the Antiviral Drug Acyclovir and Its Biodegradation Product Carboxy-acyclovir with Ozone: Kinetics and Identification of Oxidation Products. *Environmental Science & Technology*, 46(4), pp. 2169–2178. Available at: <http://pubs.acs.org/doi/10.1021/es203712z>
21. Prosser R.S. and Sibley P.K. (2015). Human health risk assessment of pharmaceuticals and personal care products in plant tissue due to biosolids and manure amendments, and wastewater irrigation. *Environment International*, 75, pp.223–233 (including corrigendum). Available at: <https://www.ncbi.nlm.nih.gov/pubmed/25486094>
22. Boxall et al. (2006). Uptake of veterinary medicines from soils into plants. *Journal of Agricultural Food and Chemistry*, 54, pp.2288–2297. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/16536609>
23. Wu et al. (2013). Comparative uptake and translocation of pharmaceutical and personal care products (PPCPs) by common vegetables. *Environment International*, 60, pp.15–22. Available at: <http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.728.2591&rep=rep1&type=pdf>

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