6

Impact of Emerging Pollutants on a Health Triad: Environment, Animals and Humans

AUTHORS DETAIL

Pablo Antonio Moreno-Pérez[1], Gauddy Lizeth Manzanares-Leal[1], Miguel Ángel Karam Calderon[1], Yazmín Castillo Sánchez[1] and Ninfa Ramírez-Durán[1*]

[1]Facultad de Medicina, Universidad Autónoma del Estado de México, Toluca, Estado de México
*Corresponding author: ninfard@hotmail.com

Received: Sept 18, 2022 **Accepted: Dec 19. 2022**

INTRODUCTION

Emerging pollutants (EP) are the compounds of anthropogenic origin that usually do not screened in the environment (Geissen et al. 2015; Teodosiu et al. 2018). EP in the environment is influenced by several factors, such as population growth, which has generated a high demand for "hazardous" chemicals for health, approximately more than 220 million tons (https://ec.europa.eu/eurostat/). EP include those of pharmaceutical origin (FEP), synthetic or natural chemical substances used as commercial prescription drugs for therapeutic and veterinary use to diagnose, cure, treat or prevent diseases in humans and animals. (WHO 2012; Nyagah et al. 2020). FEP include many analgesics, antidiabetics, antibiotics, antidepressants, steroid antihypertensives and stimulants (Schwartz et al. 2021; Turcios et al. 2021). The subministering of FEP is regulated for patient safety, but the side effect of any drug on the environment lacks regulation (Anchique et al. 2021). In general, estimated three-quarters of polluting industrial emissions are discharged into the environment without pretreatment (Vasilachi et al. 2021). Due to this situation, PEFs and their metabolites are released into the environment through treatment plants (Massima et al. 2021) and human sanitary discharges without prior treatment. The above generates a threat to the environment since chronic exposure to various pharmaceutical substances, the increase in the concentration of FEPs as they accumulate in the environment and the great variety of substances that can be found, coupled with their low biodegradability and high persistence, allows their bioaccumulation in various systems, from the lowest trophic levels to humans (Fonseca et al. 2020; Turcios et al. 2021). Because of the evidence of various FEP in the environment, intensive research on their fate and risk has generated significant interest (Mulkiewicz et al. 2021).

Impact of Emerging Pollutants on the Environment

In 2019, the global pharmaceuticals manufacturing market was estimated to be over $320 trillion (320 billion, with a compound annual growth rate of over 13% from 2020 to 2027 (Grand View Research 2020). Approximately 4000 active pharmaceutical products are manufactured and incorporated into thousands of products available in the market (Daughton 2014). The pharmaceutical product cycle consists of three main stages: manufacture, consumption, and disposal (Kusturica et al. 2020). When the manufacturing process is completed, pharmaceuticals are distributed in multiple presentations, such as tablets, capsules, and liquid formulations (Dunn et al. 2010). Once orally ingested by the body (human or animal), 30-90% is not entirely metabolized and is excreted as an active substance (Nyagah et al. 2020; O'Flynn et al. 2021), mainly through urine (70% on average) and feces (30%) (Abdel-Shafy and Mohamed-Mansour 2013; Hassan et al. 2019).

Pharmaceutical FPs can integrate into the environment through the manufacturing process, disposed or unused products, excretion by humans and animals, wastewater discharges, livestock husbandry, and leached landfill sites (Kleywegt et al. 2019; Lam et al. 2021). Although the concentrations of FEP found in the environment, have been in the ng/L and g/L ranges (Tran 2013; Ahmed et al. 2017), yet these can cause ecological disturbances (Belhaj et al. 2015), as well as adverse effects on human health. Due to the evidence of their presence in the environment, interest in their research has increased in the scientific community in recent decades (Turcios et al. 2021).

Impact of Emerging Pollutants on Animals

The administration of drugs to animals is a strategy to prevent and combat disease and maintain optimal health (CDDEP 2021). In 2010 alone, livestock consumed more than 63,000 tons of antimicrobial drugs worldwide, which will be more than 100,000 tons by 2030 (Van Boeckel et al. 2015). However, drugs administered to animals are not fully metabolized (Zhao et al. 2010). Numerous studies have

Citation: Moreno-Pérez PA, Manzanares-Leal GL, Calderon MÁK, Sánchez YC and Ramírez-Durán N, 2023. Impact of emerging pollutants on a health triad: environment, animals and humans. In: Aguilar-Marcelino L, Abbas RZ, Khan A, Younus M and Saeed NM (eds), One Health Triad, Unique Scientific Publishers, Faisalabad, Pakistan, Vol. 1, pp: 31-35. https://doi.org/10.47278/book.oht/2023.06

reported the presence of drugs such as fluoroquinolones, antibiotics, sulfonamides, and tetracyclines in animal manure samples (Qiao et al. 2012; Li et al. 2013; Hou et al. 2015; Van Epps and Blaney 2016); which may pose a threat to animal species. The transfer of drugs through food chains may interfere with other species ecological systems (Chopra and Kumar 2018).

The negative impact of PEFs on the animal body has been reported, for example, in the decline of vulture populations (*Gyps indicus*, *Gyps bengalensis*, *Gyps tenuirostris*) in countries such as Bangladesh, India, Nepal, Pakistan and Switzerland, due to poisoning with antibiotics and non-steroidal anti-inflammatory drugs (Prakash et al. 2003; Oaks et al. 2004; Swan et al. 2016). Another example is the amphipod crustacean Gammarus locusta which, exposed to simvastatin, alters its reproduction and growth (Neuparth et al. 2014). In rainbow trout (*Oncorhynchus mykiss*), this same drug causes hepatic cytotoxicity, metabolic inhibition, and cell membrane loss (Ellesat et al. 2020).

On the other hand, carbamazepine inhibits molting and growth in the crab *Eriocheir sinensis* (Chen et al. 2019). It causes malformations during embryonic development in the Mediterranean mussel *Mytilus galloprovincialis* (Franzellitti 2019), as well as alterations in motility and behavior in embryos of the zebrafish, *Danio rerio* (Weichert et al. 2017). Diclofenac, a non-steroidal anti-inflammatory drug, can cause oxidative stress and affect testosterone levels in wolf fish *Hoplias malabaricus* (Guiloski et al. 2015); cytological changes in liver, kidneys, and gills of *O. mykiss* (Schwaiger et al. 2004); lower hematocrit levels in brown trout *Salmo trutta* (Hoeger et al. 2005); toxic effects in catfish *Rhamdia quelen* (Ribas et al. 2017); ragworm, *Hediste diversicolo* and sole fish *Solea senegalensis* (Nunes et al. 2020); in tilapia *Oreochromis niloticus* (Gröner et al. 2017) and the fish Corvina, *Argyrosomus regius* (Duarte et al. 2020).

Impact of Emerging Pollutants on Humans

The availability of clean water is indispensable for human health. While considering the population and industrial growth worldwide, the need for clean water is increasing (Tortajada 2020; Lam et al. 2021). The presence of FEP threatens the supply and availability of freshwater. Various research suggests that 70% of FEP are from domestic water and 30% from industrial waste, which is discharged directly into rivers without treatment (Bunke et al. 2019; Tang et al. 2019). Even in the case of treated wastewater, the accumulation of FP does not allow its reuse, limiting the under-supply of drinking water (Massima et al. 2021). The presence of PEFs has been described in freshwater and drinking water sources, finding antibiotics and non-steroidal anti-inflammatory drugs (Fernandes et al. 2020; Khan et al. 2020; Ngqwala and Muchesa 2020). These accumulate directly in water sources, causing adverse effects on microorganisms and aquatic animals through bioaccumulation in food chains and favoring antibiotic resistance in bacteria, leading to a threat for health and safety (Hassoun-Kheir et al. 2020; Wang 2020).

Studies conducted by Savin et al. (2021) and León-Aguirre et al. (2019) in swine facilities for meat intended for human consumption found that *E. coli* bacteria presented resistance to the antibiotic's ciprofloxacin and piperacillin. They also found enrofloxacin, oxytetracycline, and sulfamethoxazole in wastewater treated by biodigesters.

The constant accumulation and under-supply of antibiotics allow the generation of resistance genes. Liang et al. (2021) identified the genes APH(3′)-IIIa, APH(6)-Id, APH(3")-Ib; OXA-347; ermF, msrE, cfrA and tetQ, tet36, tetX, tetM (resistant to aminoglycoside, β-lactam, macrolide-lincosamide-streptogramin, tetracycline respectively) from China. For their part, in swine wastewater, Suzuki et al. (2021) found the antibiotics lincomycin and tetracyclines also detected the presence of the resistance genes sul1, sul2, sul3, and tet(M), suggesting that, even if the use of antibiotics is suspended, the resistance genes remain in the environment for an extended period. The exposure of microorganisms to antibiotics can favor the generation of resistance to different antibiotics through mechanisms such as impermeable barriers, efflux pumps, drug inactivation, and mutational resistance (Allen et al. 2010). A Study by Andersson and Hughes 2014 reveal that even non-lethal levels of antibiotics in the environment can exacerbate the selection and enrichment of resistance genes.

General Information on the Removal of Emerging Pollutants

Unlike conventional contaminants, the removal of PE presents characteristics that complicate its removal. They are polar molecules; the pH of the medium affects their properties and can present variations in structure, form, and functionality. In addition, once consumed, absorbed, and eliminated, these can present changes in their chemical structure due to the previous metabolic process (Rivera-Utrilla et al. 2013). The sum of all these characteristics and the presence of different EP in the same environments makes it more complex to understand all interactions, which are not evident today.

The strategy of eliminating or removing FEP from the environment started because the natural attenuation of these compounds based on physical, chemical, and biological processes is insufficient due to the many xenobiotic compounds released. Processes for the elimination or removal of EP generally involve biological and physicochemical treatments. According to Liu et al. (2020), biological processes include Activated Sludge treatments based on coagulation, adsorption, and oxidation of sludge; Membrane Bioreactors, a process that combines microbial degradation and membrane separation; Composting based on animal manure; Phytoremediation based on microalgae; and Bacterial Bioremediation. Among the physical and physicochemical processes, there are Membrane Processes, which use porous or non-porous membranes to filter contaminants; Adsorption of mineral surfaces and ion exchange, which uses substrates such as modified natural zeolite; Carbon Adsorption, used as adsorption material; Coagulation, for the removal of non-polar molecules and the use of nanomaterials such as graphene. In addition, the same author mentions chemical oxidation, which can destroy the molecular structure of some pollutants or favor their biodegradability, such as ozone use. Ozone can react with some pollutants giving rise to a series of free radicals or produce some hydroxyl radicals to degrade the pollutants, depending on the acidity or alkalinity. Electrochemical oxidation is based on oxidation by an electrical voltage; catalysis, which includes processes such as photolysis and photocatalysis; and treatment technologies.

Although all contaminant removal treatments have advantages, they also have disadvantages. Activated sludge can be affected by temperature and pollutant types (Liu et al. 2020); membrane bioreactors by the cost of membrane materials, sludge concentration, solids retention time and organic loading (Zhen et al. 2019); composting can be influenced by temperature; ozone is only effective on some pollutants, plus it is unable to fully oxidize or mineralize them (Liu et al. 2020). Membrane processes are hindered by membrane flux, pore size, hydrophobicity, and molecular weight of the pollutant, and adsorption from mineral surfaces and ion exchange present low capacity and poor selectivity. Carbon adsorption depends on the surface area, pore structure, and functional surface (Xing et al. 2019; Zhang et al. 2019); electrochemical oxidation quickly produces degradation intermediates and electrode deactivation (Tasca et al. 2019) and catalysis is influenced by the pH value of the solution, type of light source and own characteristics of the catalysts (Carena et al. 2019). The results of the investigations have shown that the removal of EP is generally not completely efficient.

Removal of Emerging Pollutants from Pharmaceuticals

The main treatments to remove or eliminate FEP include collection for subsequent incineration, collection in ordinary dumpsters, and discharge into the sewage system for subsequent wastewater treatment (Bu et al. 2020). These treatments have advantages and disadvantages; incineration presents destruction and a significant reduction of waste volume (Ghasemi and Yusuff 2016; Trinh et al. 2020) but can release heavy metals into the atmosphere (Sabiha-Javied et al. 2008); in addition to the cost associated with the design and construction of these facilities. The collection in ordinary dumpsters uses specific sites to deposit waste and isolate it from the surrounding environment (Narayana 2009). However, due to the increased pharmaceutical production and volume disposed of, the designated areas are insufficient, so the drugs are leached. Previous studies have detected a complex mixture of contaminants, including FEP, in multiple landfills in 100 to 1,000,000 ng/L (Masoner 2014). The wastewater treatment process has proven to be efficient, mainly for removing conventional contaminants, such as biodegradables, organic matter, and nutrients, but it is not efficient for removing pharmaceuticals (Kümmerer 2008; Sim et al. 2010).

Conclusion

The process of manufacturing, distribution, consumption, and disposal of FEP is a polluting phenomenon for the environment, animals, and humans. The complex mixture of diverse FEP threatens the environmental impact in diverse ecosystems. Some of the alternatives to diminish this impact on the health triad are to initiate the process of regulating FEP in the environment, establish control, management, and distribution laws, as well as permanent monitoring of the diverse ecosystems related to the presence of FEP, promote international research in remediation processes with new technologies, as well as the use of common treatment methods.

REFERENCES

Abdel-Shafy HI and Mohamed-Mansour MS, 2013. Issue of pharmaceutical compounds in water and wastewater: Sources, impact and elimination. Egyptian Journal of Chemistry 56 (5–6): 449–471.

Ahmed MB et al., 2017. Progress in the Biological and Chemical Treatment Technologies for Emerging Contaminant Removal from Wastewater: A Critical Review. Journal of Hazardous Materials 323: 274–298.

Allen HK et al., 2010. Call of the wild: antibiotic resistance genes in natural environments. Nature Reviews Microbiology 8: 251–259.

Anchique L et al., 2021. Predicting the Adsorption of Amoxicillin and Ibuprofen on Chitosan and Graphene Oxide Materials: A Density Functional Theory Study. Polymers 13: 1620.

Andersson DI and Hughes D, 2014. Microbiological effects of sublethal levels of antibiotics. Nature Reviews Microbiology 12: 465–478.

Belhaj D et al., 2015. Fate of Selected Estrogenic Hormones in an Urban Sewage Treatment Plant in Tunisia (North Africa). Science of The Total Environment 505: 154–160.

Bu Q, 2020. Is disposal of unused pharmaceuticals as municipal solid waste by landfilling a good option? A case study in China. Bulletin of Environmental Contamination and Toxicology 105: 784–789.

Bunke D et al., 2019. Developments in society and implications for emerging pollutants in the aquatic environment. Environmental Sciences Europe 31: 1–17.

Carena L et al., 2019. Environmental photodegradation of emerging contaminants: A reexamination of the importance of triplet-sensitised processes, based on the use of 4-carboxybenzophenone as proxy for the chromophoric dissolved organic matter. Chemosphere 237: 124476.

CDDEP, 2021. The State of the World's Antibiotics 2021: a Global Analysis of Antimicrobial Resistance and its Drivers.

Chen H et al., 2019. Carbamazepine disrupts molting hormone signaling and inhibits molting and growth of Eriocheir sinensis at environmentally relevant concentrations. Aquatic Toxicology 208: 38–145.

Chopra S and Kumar D, 2018. Pharmaceuticals and Personal Care Products (PPCPs) as Emerging Environmental Pollutants: Toxicity and Risk Assessment. In: Gahlawat, Advances in Animal Biotechnology and its Applications. Springer, Singapore.

Daughton CG, 2014. Eco-directed sustainable prescribing: feasibility for reducing water contamination by drugs. Science of The Total Environment 493: 392–404.

Duarte IA et al., 2020. Depressed, hypertense and sore: longterm effects of fluoxetine, propranolol and diclofenac exposure in a top predator fish. Science of The Total Environment 712: 136564.

Dunn PJ et al., 2010. Green chemistry in the pharmaceutical industry. In: Dunn, P.J., Wells, A.S., Williams, M.T. (Eds.), Green Chemistry in the Pharmaceutical Industry. Wiley-VCH Verlag GmbH & Co. KGaA.

Ellesat KS et al., 2020. Cytotoxicity of atorvastatin and simvastatin on primary rainbow trout (Oncorhynchus mykiss) hepatocytes. Toxicolgy In Vitro 24: 1610–1618.

Fernandes MJ et al., 2020. Antibiotics and antidepressants occurrence in surface waters and sediments collected in the north of Portugal. Chemosphere 239.

Fonseca VF et al., 2020. Roving Pharmacies: Modelling the Dispersion of Pharmaceutical Contamination in Estuaries. Ecological Indicators 115: 106437.

Franzellitti S, 2019. Microplastic exposure and effects in aquatic organisms: A physiological perspective. Environmental Toxicology and Pharmacology 68: 37–51.

Geissen V et al., 2015. Emerging pollutants in the environment: A challenge for water resource management. International Soil and Water Conservation Research 3: 57–65.

Ghasemi MK and Yusuff RBM, 2016. Advantages and disadvantages of healthcare waste treatment and disposal alternatives: Malaysian scenario. Polish Journal of Environmental Studies 25: 17–25.

Grand View Research, 2020. Pharmaceutical Manufacturing Market Size, Share & Trends Analysis Report By Drug Development Type, By Formulation, By Route Of Administration, By Therapy Area, By Prescription, By Age Group, And Segment Forecasts, 2020-2027.

Gröner F et al., 2017. Chronic diclofenac exposure affects gill integrity and pituitary gene expression and displays estrogenic activity in nile tilapia (Oreochromis niloticus). Chemosphere 166: 473–481.

Guiloski IC et al., 2015. Effects of trophic exposure to dexamethasone and diclofenac in freshwater fish. Ecotoxicology and Environmental Safety 114: 204–211.

Hassan SSM et al., 2019. Removal of pharmaceutical compounds from urine via chemical coagulation by green synthesized ZnO-nanoparticles followed by microfiltration for safe reuse. Arabian Journal of Chemistry 12: 4074–4083.

Hassoun-Kheir N et al., 2020. Comparison of antibiotic-resistant bacteria and antibiotic resistance genes abundance in hospital and community wastewater: A systematic review. Science of The Total Environment 743: 140804.

Hoeger B et al., 2005. Water-borne diclofenac affects kidney and gill integrity and selected immune parameters in brown trout (Salmo trutta f. fario). Aquatic Toxicology 75: 53–64.

Hou J et al., 2015. Occurrence and distribution of sulfonamides, tetracyclines, quinolones, macrolides, and nitrofurans in livestock manure and amended soils of Northern China. Environmental Science and Pollution Research 22: 4545–4554.

Khan HK et al., 2020. Fate and toxicity of pharmaceuticals in water environment: An insight on their occurrence in South Asia. Journal of Environmental Management 271.

Kleywegt S et al., 2019. Environmental loadings of active pharmaceutical ingredients from manufacturing facilities in Canada. Science of the Total Environment 646: 257– 264.

Kümmerer K, 2008. Pharmaceuticals in the Environment: Source, Fate, Effects and Risk K. Kümmerer (ed.); Third, Vol. 53, Issue 9). Springer-Verlag Berlin Heidelberg.

Kusturica MP et al., 2020. Consumer willingness to pay for a pharmaceutical disposal program in Serbia: a double hurdle modeling approach. Waste Management 104: 246–253.

Lam VT et al., 2021. Facile Fabrication of Novel NiFe2O4@Carbon Composites for Enhanced Adsorption of Emergent Antibiotics. Materials 14: 6710.

León-Aguirre K et al., 2019. A Rapid and Green Method for the Determination of Veterinary Pharmaceuticals in Swine Wastewater by Fluorescence Spectrophotometry. Bulletin of Environmental Contamination and Toxicology 103: 610-616.

Li YX et al., 2013. The residues and environmental risks of multiple veterinary antibiotics in animal faeces. Environmental Monitoring and Assessment 185: 2211–2220.

Liang C et al., 2021. Removal of antibiotic resistance genes from swine wastewater by membrane filtration treatment. Ecotoxicology and Environmental Safety 2010.

Liu B et al., 2020. Emerging pollutants—Part II: Treatment. Water Environment Research 92: 1603– 1617.

Masoner JR, 2014. Contaminants of emerging concern in fresh leachate from landfills in the conterminous United States. Environmental Science: Processes and Impacts 16: 2335–2354.

Massima ES et al., 2021. Removal of Pharmaceutical Residues fromWater andWastewater Using Dielectric Barrier Discharge Methods—A Review. International Journal of Environmental Research and Public Health 18: 1683.

Mulkiewicz E et al., 2021. Metabolism of non-steroidal anti-inflammatory drugs by non-target wild-living organisms. Science of The Total Environment 791: 148251.

Narayana T, 2009. Municipal solid waste management in India: From waste disposal to recovery of resources? Waste Manager 29: 1163–1166.

Neuparth T et al., 2014. Hypocholesterolaemic pharmaceutical simvastatin disrupts reproduction and population growth of the amphipod Gammarus locusta at the ng/L range. Aquatic Toxicology 155: 337–347.

Ngqwala NP and Muchesa P, 2020. Occurrence of pharmaceuticals in aquatic environments: A review and potential impacts in South Africa. South African Journal of Science 116.

Nunes B et al., 2020. Toxic effects of environmentally realistic concentrations of diclofenac in organisms from two distinct trophic levels, Hediste diversicolor and Solea senegalensis. Comparative Biochemistry and Physiology Part C 231.

Nyagah DM, 2020. Pharmaceutical Waste: Overview, Management, and Impact of Improper Disposal. Preprints 2020100245.

O'Flynn D et al., 2021. A review of pharmaceutical occurrence and pathways in the aquatic environment in the context of a changing climate and the COVID-19 pandemic. Analytical Methods Journal 13: 575–594.

Oaks JL et al., 2004. Diclofenac residues as the cause of vulture population decline in Pakistan. Nature 427: 630–633.

Prakash V et al., 2003. Catastrophic collapse of indian white-backed Gyps bengalensis and long-billed Gyps indicus vulture populations. Biological Conservation 109: 381–390.

Qiao M et al., 2012. Fate of tetracyclines in swine manure of three selected swine farms in China. Journal of Environmental Sciences 24: 1047–1052.

Ribas JLC et al., 2017. Inhibition of immune responses and related proteins in Rhamdia quelen exposed to diclofenac. Environmental Toxicology and Chemistry 36: 2092–2107.

Rivera-Utrilla J et al., 2013. Pharmaceuticals as emerging contaminants and their removal from water. A review. Chemosphere 93: 1268–1287.

Sabiha-Javied et al., 2008. Heavy metal pollution from medical waste incineration at Islamabad and Rawalpindi, Pakistan. Microchemical Journal 90: 77–81.

Savin M et al., 2021. Clinically Relevant Escherichia coli Isolates from Process Waters and Wastewater of Poultry and Pig Slaughterhouses in Germany. Microorganisms 9: 698.

Schwaiger J et al., 2004. Toxic effects of the non-steroidal anti-inflammatory drug diclofenac. Part I: histopathological alterations and bioaccumulation in rainbow trout. Aquatic Toxicology 68: 141–150.

Schwartz H et al., 2021. Pharmaceuticals in source waters of 95 First Nations in Canada. Canadian Journal of Public Health 112: 133–153.

Sim WJ et al., 2010. Occurrence and fate of pharmaceuticals in wastewater treatment plants and rivers in Korea. Environmental Pollution 158: 1938–1947.

Suzuki S et al., 2021. Contamination of antibiotics and sul and tet(M) genes in veterinary wastewater, river, and coastal sea in Thailand. Science of The Total Environment 791: 148423.

Swan GE et al., 2006. Toxicity of diclofenac to Gyps vultures. Biology Letters 2: 279–282.

Tang Y et al., 2019. Emerging pollutants in water environment: Occurrence, monitoring, fate, and risk assessment. Water Environment Research 91: 984–991.

Tasca AL et al., 2019. Electrochemical removal of Terbuthylazine: Boron-Doped Diamond anode coupled with solid polymer electrolyte. Environmental Pollution 251: 285–291.

Teodosiu C et al., 2018. Emerging Pollutants Removal through Advanced Drinking Water Treatment: A Review on Processes and Environmental Performances Assessment. Journal of Cleaner Production 197: 1210–1221.

Tortajada C, 2020. Contributions of recycled wastewater to clean water and sanitation Sustainable Development Goals. NPJ Clean Water 3.

Tran NH, 2013. Insight into Metabolic and Cometabolic Activities of Autotrophic and Heterotrophic Microorganisms in the Biodegradation of Emerging Trace Organic Contaminants. Bioresource Technology 146: 721–731.

Trinh VT et al., 2020. Treatment of medical solid waste using an Air Flow controlled incinerator. Polish Journal of Chemical Technology 22: 29–34.

Turcios AE et al., 2021. Screening of Emerging Pollutants (EPs) in Estuarine Water and Phytoremediation Capacity of Tripolium pannonicum under Controlled Conditions. International Journal of Environmental Research and Public Health 18: 943.

Van Boeckel TP et al., 2015. Global trends in antimicrobial use in food animals. Proceedings of the National Academy of Sciences. Proceedings of the National Academy of Sciences of the United States of America, pp: 5649–5654.

Van Epps A and Blaney L, 2016. Antibiotic residues in animal waste: occurrence and degradation in conventional agricultural waste management practices. Current Pollution Reports 2: 135–155.

Vasilachi IC et al., 2021. Review. Occurrence and fate of emerging pollutants in wáter environmental and options for their removal. Water 13: 181.

Wang J, 2020. Occurrence and fate of antibiotics, antibiotic resistant genes (ARGs) and antibiotic resistant bacteria (ARB) in municipal wastewater treatment plant: An overview. Science of The Total Environment 744: 140997.

Weichert FG et al., 2017. Assessing the ecotoxicity of potentially neurotoxic substances-Evaluation of a behavioural parameter in the embryogenesis of Danio rerio. Chemosphere 186: 43–50.

WHO, 2012. World Health Organization. Pharmaceuticals in Drinking Water. doi: https://doi.org/10.1016/B978-0-444-52272-6.00457-8.

Xing J et al., 2019. Organic matter removal and membrane fouling mitigation during algae-rich surface water treatment by powdered activated carbon adsorption pretreatment: Enhanced by UV and UV/chlorine oxidation. Water Research 159: 283–293.

Zhang P et al., 2019. Microwave-assisted chemical modification method for surface regulation of biochar and its application for estrogen removal. Process Safety and Environment Protection 128: 329–341.

Zhao L et al., 2010. Residues of veterinary antibiotics in manures from feedlot livestock in eight provinces of China. Science of The Total Environment 408: 1069–1075.

Zhen G et al., 2019. Anaerobic membrane bioreactor towards biowaste biorefinery and chemical energy harvest: Recent progress, membrane fouling and future perspectives. Renewable Sustainable Energy Reviews 115: 109392.