REV. INVESTIG. ALTOANDIN

http://dx.doi.org/10.18271/ria.2018.365

Journal of High Andean Research, 2018; 20(2): 215 - 224

Contenido: http://huajsapata.unap.edu.pe/ria/index.php/ria/issue/archive

Revista de Investigaciones Altoandinas

Periodo **Abril - Junio -** ISSN: 2306-8582 (V. impresa) - ISSN: 2313-2957 (V. digital)

Antibiotics and their environmental implications

Antibióticos y su implicancia ambiental

Franz Zirena Vilca[1*], Wildor Gosgot Angeles[2], Edith Tello Palma[3], Clara Nelly Campos Quiroz[2], Teofilo Donaires Flores[3] & Walter Alejandro Zamalloa Cuba[3]

[1]Escuela de Posgrado de la Universidad Nacional del Altiplano, Puno-Perú.
[2]Universidad Nacional Toribio Rodríguez de Mendoza de Amazonas, Calle Higos Urco N° 342-350-356, Calle Universitaria N° 304, Chachapoyas – Amazonas-Perú.
[3]Escuela Profesional de Ingeniería Química de la Universidad Nacional del Altiplano, Av Floral S/N Puno-Perú.
*Autor para correspondencia, e-mail: franzvilca@usp.br

REVIEW ARTICLE

ARTICLE INFORMATION

Received 13-11-2017
Accepted 31-03-2018
On line: 27-04-2018

KEY WORDS:

Toxicology, emerging pollutant and water.

ABSTRACT

Due to its extensive use in various livestock production activities and its use in human health care, antibiotics have become an environmental problem that draws the attention of the scientific community. Several research works report their presence in different ecosystems compartments, as well as their impact in organisms that inhabit these ecosystems which are being investigated by this community; until now, it has been reported problems of bacterial resistance and damages at DNA level in living beings, among others; in this perspective it is necessary to perform monitoring in various environmental matrixes, in order to detect and quantify their presence, to have a better understanding of their long-term effects on living beings. In this sense, it addresses aspects that determine their presence in the ecosystem, as well as shows results of works evaluating their removal of contaminated water, in order to ensure their safety from an environmental perspective and taking into consideration the health of living beings and human beings.

ARTÍCULO DE REVISIÓN

INFORMACIÓN DEL ARTÍCULO

Recibido 13-11-2017
Aceptado 31-03-2018
On line: 27-04-2018

PALABRAS CLAVES:

Toxicología, contaminante emergente y agua.

RESUMEN

Debido a su amplio uso en diversas actividades de producción de ganado y su uso en el cuidado de la salud humana, los antibióticos, se han convertido en un problema ambiental que llama la atención de la comunidad científica. Diversos trabajos reportan su presencia en diversos compartimientos de los ecosistemas, así como su impacto a los organismos que habitan estos ecosistemas se encuentran siendo investigados por esta comunidad, hasta el momento se han reportado problemas de resistencia bacteriana y daños a nivel de ADN en seres vivos, entre otros, por lo que, se hace necesario realizar el monitoreo en diversas matrices ambientales, con el fin de detectar y cuantificar su presencia, para tener un mejor conocimiento de su efectos a largo plazo en seres vivos. En ese sentido, se abordan aspectos que determinan su presencia en el ecosistema, así como se muestra resultados de trabajos que evalúan su remoción de aguas contaminadas, con el fin de garantizar su seguridad desde una perspectiva ambiental y llevando en consideración la salud de seres vivos y del mismo ser humano.

1. INTRODUCTION

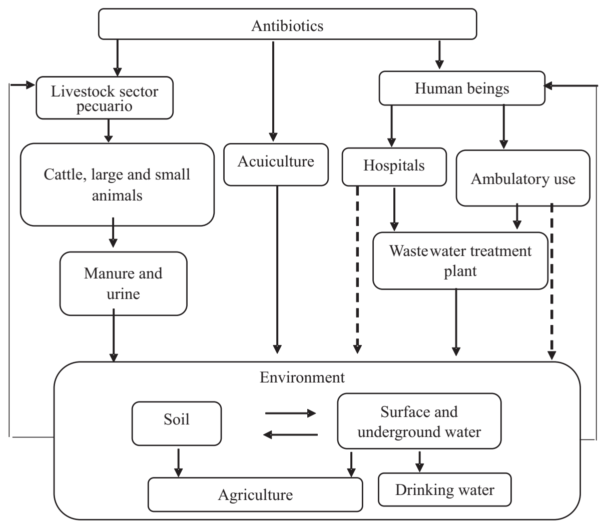
Population growth and increased urbanization, as well as industrialization (Zhang et al., 2017), have increased the demand for animal protein for human consumption (Boeckel et al., 2015), therefore, the livestock sector in South America has grown at an annual rate of 3.7 %, higher than the average global growth rate of 2.1 %, becoming the region with the largest export of beef and poultry (FAO, 2017), the intensive use of the productive systems of poultry, pigs and dairy cattle at large scale (Van et al., 2017). These activities are demanding the use of veterinary products for the treatment of diseases, such as lumpy skin (Molla, Frankea, Gari, & de Jong, 2017), protozoan, bacterial, viral, helminthiasis, nutritional and others (Byaruhanga et al., 2017); antibiotics are also used for the treatment and prevention of diseases in humans (Kim, Lee, & Oh, 2017).

On the other hand, 54 % of the deaths of people in 2015 were caused by diseases such as ischemic heart disease, lung cancer, diabetes, diarrhoeal diseases, tuberculosis, among others, which have been treated in hospital centers based of antibiotics (WHO, 2017), although, there are patients who self-medicated using antibiotics excessively because of their availability and low cost(OMS, 2016).

The consumption of antibiotics is causing serious impacts on the environment (Carvalho & Santos, 2016), because between 30 to 90 % of the antibiotics administered in the livestock system are not metabolized (Aminov, 2010); and 70 % of the dose of antibiotics applied in humans are eliminated (Butkovskyi, Hernandez, Rijnaarts, & Zeeman, 2015) to the natural ecosystems (Aminov, 2010); mainly the aquatic ecosystem, affecting its functions of mineralization and decomposition of organic matter, as well as the degradation of organic pollutants (Bergeron, Boopathy, Nathaniel, Corbin, & La Fleur, 2015; von et al., 2017,); on the other hand, these compounds cause impacts on soil microbiota (Zhang & Dick, 2014) and groundwater (Pan & Chu, 2017).

2. ANTIBIOTIC SOURCES IN THE ENVIRONMENT

The presence and persistence of antibiotics in the aquatic environment is a worldwide concern (Fram & Belitz, 2011; von Schiller et al., 2017), because they are widely used in animal production (Tasho & Cho, 2016), aquaculture and agriculture (Jiang, Zhou, Yang, Chen, & Cheng, 2017). Antibiotics are disseminated mainly through direct and indirect emissions such as excrement, sewage irrigation and sludge compost, getting into the environment negatively impacting soil ecosystems (Li et al., 2015; Shi, Yue, Du, Wang, & Li, 2016) and Agua (Vo et al., 2016), as it is shown in graph 1, the interaction of antibiotics and the environment.



Graph 1. Antibiotic sources

2.1. Humans

Gothwal & Shashidhar (2015) suggest that antibiotics used for the treatment of diseases in human health are classified according to their mechanism of action such as β-lactams, sulfonamides, monobactams, carbapenem, aminoglycosides, glycopeptide, lincomycin, macrolides, polypeptides, polyenos, rifamycin, tetracyclines, chloramphenicol, quinolones and fluoroquinolones.

Unfortunately, the misuse of these products brings bacterial resistance problems (Villalobos, Barrero, Rivera, Ovalle, and Valera, 2013), that is the case of the enteric bacteria and the fecal coliform bacteria (Mudryk et al., 2013), causing public health problems such as infections (Magdaleno et al., 2012; Peña-Álvarez & Castillo-Alanise, 2015).

2.1.1. Wastewater treatment plants

70 % of the dose of antibiotics applied in humans are eliminated through urine and feces (Ikehata, Jodeiri, & Gamal El-Din, 2006; Butkovskyi et al., 2015), which may contain different active compounds and metabolites (Klatte, Schaefer, & Hempel, 2017) that are discharged into wastewater (Özcan, Özcan, & Demirci, 2016) causing ecological damage (Baquero, Martínez, & Canton, 2008; Liu et al., 2013; Padilla-Robles et al., 2015).

Domestic wastewater is arranged in treatment plants (WWTP) (Nnadozie, Kumari, & Bux, 2017), where they undergo three stages: preliminary, primary (physical-chemical) and secondary (biological) (Verlicchi, Al Aukidy, & Zambello, 2012); However, these treatments are not effective in the removal of organic contaminants that are present in these waters (Batt, Bruce, & Aga, 2006); Because WWTPs are not designed to remove these substances (Marx et al., 2015). Some studies show the presence of up to seven groups of antibiotics in the tributaries and effluents of the WWTPs, sulfamethoxazole (2.5 ± 1.9 $\mu g\ L^{-1}$), norfloxacin (9.6 ± 9.8 $\mu g\ L^{-1}$), ciprofloxacin (5.3 ± 4.8 $\mu g\ L^{-1}$), ofloxacin (10.9 ± 8.1 $\mu g\ L^{-1}$), erythromycin (1.2 ± 1.2 $\mu g\ L^{-1}$), tetracycline (0.1 ± 0.0 $\mu g\ L^{-1}$), and trimenthoprim (1.0 ± 0.9 $\mu g\ L^{-1}$) (Vo et al., 2016) (Li, Jianman, Cheng, Weixiao, Xu, Like, Jiao, Yanan, Ali Baig, Shams, 2015) (singer et al., 2014).

The main factors that are influencing the final concentration of antibiotics in the environment are: prolonged sludge retention time (SRT), hydraulic retention time (HRT) (Nnadozie et al., 2017); operating temperature (Le-Minh, Khan, Drewes, & Stuetz, 2010); oxygen concentration, amount of substrate (sludge) (Rizzo et al., 2013); coexistence of microbial pathogens in WWTPs; as well as seasonality and common infectious diseases, forming a complex cycle of transformation and bioaccumulation, causing toxicity to human health (Carvalho & Santos, 2016) (Pan & Chu, 2017a) and aquatic ecotoxicity (Ternes et al., 2017).

2.2. Livestock

It has been estimated that between 30 to 90 % of antibiotics administered to animals are excreted through manure and urine (Aminov, 2010), reaching concentrations of up to 66.5 $\mu g\ kg^{-1}$ in swine manure, 15.7 $\mu g\ kg^{-1}$ in chicken manure and 1.6 $\mu g\ kg^{-1}$ in cattle manure (Martínez-Carballo et al., 2007). The waste is released directly to the environment by runoff processes, whilst leaching reach the water bodies causing eutrophication and bacterial resistance (Drogui, 2013).

2.3. Aquaculture

The use of antibiotics in aquaculture is intended for the prevention of infectious diseases in fish (Santos & Ramos, 2016). The most widely used antibiotics in this sector are: oxytetracycline, oxolinic acid, chloramphenicol and tetracycline which comprises about 40 % of the consumption (Sapkota et al., 2008; Donate, Venkatesan, & Halden, 2015). Therefore, aquaculture is a potential consumer of antibiotics due to intensive fish production (he et al., 2017). For example, in Chile during 2003, it was used 0.005 kg of antibiotic for each kg of salmon produced, whilst Norway as the second leading exporter of aquaculture products, used 0.002 kg of antibiotic per kg of salmon (Done et al., 2015).

3. ENVIRONMENTAL IMPACT OF ANTIBIOTICS

3.1. Impact on water

Sui et al., (2015) determined concentrations of 2.1 and

124.5 ng L^{-1} of sulfonamide, as well as Boxall et al., (2003), Sulfadiazine and oxytetracycline with concentrations of 0.001 and 145 µg L^{-1} respectively in water bodies. The constant presence of these pollutants generates bacterial resistance (Pan-American Health Organization, 2015). In addition, alterations in plant growth (Zhang, Ying, Pan, Liu, & Zhao,2015), and modification of the structure in bacterial communities and inhibit the process of nitrate reduction, due to elevated levels of sulfamethoxazole (SMX) Underwood et al., (2011). Therefore, studies are underway to quantify acute toxicity and its effect on reproduction (Bundschuh et al., 2016) and antibacterial resistance affecting the population of macro-invertebrates (beard-Alvarez, Lance-Hawthorn, Contreras-Ramos, & González-Mora, 2013), likewise, to determine which antibiotics and to which concentrations cause toxicity in macro-invertebrates of aquatic ecosystems (Grenni, Ancona, and Barra Caracciolo, 2017).

Considerable interest has been developed on the importance of the presence of pharmaceutical products in potable water (Cui et al., 2016) and its possible long-term alterations which may cause adverse health effects in humans and animals (Archer, Petrie, Kasprzyk-Hordern, & Wolfaardt, 2017) or public health conditions (Cunha & Fernandes, 2010), as allergic reactions (Kümmerer, 2009), as well as toxic effects that reach aquatic life (Nieto, Borrull, Marce, & Pocurull, 2007).

3.2 Impact on soil

It is estimated that between 75 and 90 % of these unmetabolized products in the organisms of animals are excreted through manure (FAO, 2017). This manure is applied to the soil as fertilizer; however, the active constituents of antibiotics are not biodegraded (Li et al., 2015; Shi et al., 2016) since they are persistent in the environment (Koba et al., 2017), this generates negative impacts on the micro biota of the soil, which meet important processes (Jechalke et al., 2014), such as the breakdown of organic matter, availability of nutrients and fertility (Duchene, Vian, & Celette, 2017). In addition, the pollution of soils by antibiotics has favored the increase of resistant genes in the environment (Chen et al., 2017); likewise, the bodies of groundwater are at contamination risk because these compounds have the property of leaching during rain processes (Pan & Chu, 2017).

4. IMPORTANCE OF ANTIBIOTIC MONITORING

Due to the impact that antibiotics are causing in different ecosystems, it is necessary to determine the levels of pollution of the environment to improve the current state of knowledge about its origin, transport, destiny and effects (Ternes, Joss, & Oehlmann, 2015). On the other hand, risk assessment is an essential tool that becomes an important global concern in the field of public health and the problem of food safety (Reynaud & Deschaux, 2006). Therefore, water and soil monitoring must be applied, as part of the biological-based transition (Werbeloff, Brown, & Loorbach, 2016), applying a variety of interactions patterns (Poel, 2003) making the execution of surveillance actions, and control of resources through monitoring could allow the assessment of the quality, determining the contaminants contained in the water body (ANA, 2016), identified with priority the relevant aspects in the water field through each monitoring strategy (Murphy, Post, Buckley, Lippincott, & Robson, 2012).

5. CONCLUSION

There is a real and concerning presence of antibiotic residues in the environment, and the impact is affecting the functions of the soil and water ecosystems and moreover the organisms that inhabit them.

Short-term negative impacts such as the disappearance of bacteria populations and long-term bacterial resistance problems have been reported; on the other hand, wastewater treatment plants do not have the capacity to remove these compounds, becoming a major source of pollution for water bodies.

Acknowledgement

The authors would like to say thank you to the following students: Vela Tafur Cristian, Vargas Lucero Patricia Jhuliana, Silva Lopez Elita, Puerta Tuestas Carmen Elvira, Perez Ocampo Jhordy and Herrera Chavez Lesly Llocely. For their help.

REFERENCES

Aminov, R. I. (2010). A brief history of the antibiotic era: Lessons learned and challenges for the future. *Frontiers in Microbiology*, *1*(DEC), 1–7. doi:10.3389/fmicb.2010.00134

ANA. (2016). Protocolo Nacional para el Monitoreo de la Calidad de los Recursos Hídricos Superficiales.

Archer, E., Petrie, B., Kasprzyk-Hordern, B., & Wolfaardt, G. M. (2017). The fate of pharmaceuticals and personal care products (PPCPs), endocrine disrupting contaminants (EDCs), metabolites and illicit drugs in a WWTW and environmental waters. *Chemosphere*, *174*, 437–446.doi:10.1016/j.chemosphere.2017.01.101

Baquero, F., Martínez, J. L., & Cantón, R. (2008). Antibiotics and antibiotic resistance in water environments. *Current Opinion in Biotechnology*, *19*(3), 260–265. doi:10.1016/j.copbio.2008.05.006

Barba-Álvarez, R., De La Lanza-Espino, G., Contreras-Ramos, A., & González-Mora, I. (2013). Insectos acuáticos indicadores de calidad del agua en México: Casos de estudio, ríos Copalita, Zimatán y Coyula, Oaxaca. *Revista Mexicana de Biodiversidad*, *84*(1), 381–383. doi:10.7550/rmb.31037

Batt, A. L., Bruce, I. B., & Aga, D. S. (2006). Evaluating the vulnerability of surface waters to antibiotic contamination from varying wastewater treatment plant discharges. *Environmental Pollution*, *142*(2), 295–302. doi:10.1016/j.envpol.2005.10.010

Bergeron, S., Boopathy, R., Nathaniel, R., Corbin, A., & LaFleur, G. (2015). Presence of antibiotic resistant bacteria and antibiotic resistance genes in raw source water and treated drinking water. *International Biodeterioration and Biodegradation*, *102*, 370–374.doi:10.1016/j.ibiod.2015.04.017

Boxall, A. B. A., Fogg, L. A., Kay, P., Blackwell, P. A., Pemberton, E. J., & Croxford, A. (2003). Prioritisation of veterinary medicines in the UK environment. *Toxicology Letters*, *142*(3), 207–218. doi:10.1016/S0378-4274(03)00067-5

Bundschuh, M., Hahn, T., Ehrlich, B., Höltge, S., Kreuzig, R., & Schulz, R. (2016). Acute Toxicity and Environmental Risks of Five Veterinary Pharmaceuticals for Aquatic Macroinvertebrates. *Bulletin of Environmental Contamination and Toxicology*, *96*(2), 139–143. doi:10.1007/s00128-015-1656-8

Butkovskyi, A., Hernandez Leal, L., Rijnaarts, H. H. M., & Zeeman, G. (2015). Fate of pharmaceuticals in full-scale source separated sanitation system. *Water Research*, *85*, 384–392. doi:10.1016/j.watres.2015.08.045

Byaruhanga, J., Tayebwa, D. S., Eneku, W., Afayoa, M., Mutebi, F., Ndyanabo, S., … Vudriko, P. (2017). Retrospective study on cattle and poultry diseases in Uganda. *International Journal of Veterinary Science and Medicine*. doi:10.1016/j.ijvsm.2017.07.001

Carvalho, I. T., & Santos, L. (2016). Antibiotics in the aquatic environments: A review of the European scenario. *Environment International*. Elsevier Ltd. doi:10.1016/j.envint.2016.06.025

Chen, Q. L., An, X. L., Li, H., Zhu, Y. G., Su, J. Q., & Cui, L. (2017). Do manure-borne or indigenous soil microorganisms influence the spread of antibiotic resistance genes in manured soil? *Soil Biology and Biochemistry*, *114*, 229–237. doi:10.1016/j.soilbio.2017.07.022

Cui, C., Jin, L., jiang, L., Han, Q., Lin, K., Lu, S., … Cao, G. (2016). Removal of trace level amounts of twelve sulfonamides from drinking water by UV-activated peroxymonosulfate. *Science of The Total Environment*, *572*, 244–251. doi:10.1016/j.scitotenv.2016.07.183

Cunha, S. C., & Fernandes, J. O. (2010). Development and validation of a method based on a QuEChERS procedure and heart-cutting GC-MS for determination of five mycotoxins in cereal products. *Journal of Separation Science*, *33*(4–5), 600–609. doi:10.1002/jssc.200900695

Done, H. Y., Venkatesan, A. K., & Halden, R. U. (2015). Does the Recent Growth of Aquaculture Create Antibiotic Resistance Threats Different from those Associated with Land Animal Production in Agriculture? *The AAPS Journal*, *17*(3), 513–524. doi:10.1208/s12248-015-9722-z

Drogui, R. D. P. (2013). Tetracycline antibiotics in the environment : a review, 209–227. doi:10.1007/s10311-013-0404-8

Duchene, O., Vian, J. F., & Celette, F. (2017). Intercropping with legume for agroecological cropping systems: Complementarity and facilitation processes and the importance of soil microorganisms. A review. *Agriculture, Ecosystems and Environment*, *240*, 148–161. doi:10.1016/j.agee.2017.02.019

FAO. (2017). Producción pecuaria en América Latina y el Caribe | Oficina Regional de la FAO para América Latina y el Caribe | Organización de las Naciones Unidas para la Alimentación y la Agricultura. Recuperado de

Fram, M. S., & Belitz, K. (2011). Occurrence and concentrations of pharmaceutical compounds in groundwater used for public drinking-water supply in California. *Science of the Total Environment*, *409*(18), 3409–3417. doi:10.1016/j.scitotenv.2011.05.053

Grenni, P., Ancona, V., & Barra Caracciolo, A. (2017). Ecological effects of antibiotics on natural ecosystems: A review. *Microchemical Journal*. doi:10.1016/j.microc.2017.02.006

He, X., Xu, Y., Chen, J., Ling, J., Li, Y., Huang, L., Xie, G. (2017). Evolution of corresponding resistance genes in the water of fish tanks with multiple stresses of antibiotics and heavy metals. *Water Research*, *124*, 39–48. doi:10.1016/j.watres.2017.07.048

Ikehata, K., Jodeiri Naghashkar, N., & Gamal El-Din, M. (2006). Degradation of Aqueous Pharmaceuticals by Ozonation and Advanced Oxidation Processes: A Review. *Ozone: Science & Engineering*, *28*(6), 353–414. doi:10.1080/01919510600985937

Jechalke, S., Heuer, H., Siemens, J., Amelung, W., & Smalla, K. (2014). Fate and effects of veterinary antibiotics in soil. *Trends in Microbiology*, *22*(9), 536–545. doi:10.1016/j.tim.2014.05.005

Jiang, H., Zhou, R., Yang, Y., Chen, B., & Cheng, Z. (2017). Characterizing the antibiotic resistance genes in a river catchment: Influence of anthropogenic activities. *Journal of Environmental Sciences*, 1–8. doi:10.1016/j.jes.2017.08.009

Kim, H. Y., Lee, I. S., & Oh, J. E. (2017). Human and veterinary pharmaceuticals in the marine environment including fish farms in Korea. *Science of the Total Environment*, *579*, 940–949. doi:10.1016/j.scitotenv.2016.10.039

Klatte, S., Schaefer, H. C., & Hempel, M. (2017). Pharmaceuticals in the environment – A short review on options to minimize the exposure of humans, animals and ecosystems. *Sustainable Chemistry and Pharmacy*, *5*, 61–66. doi:10.1016/j.scp.2016.07.001

Koba, O., Golovko, O., Kodešová, R., Fér, M., & Grabic, R. (2017). Antibiotics degradation in soil: A case of clindamycin, trimethoprim, sulfamethoxazole and their transformation products. *Environmental Pollution*, *220*, 1251–1263. doi:10.1016/j.envpol.2016.11.007

Kümmerer, K. (2009). The presence of pharmaceuticals in the environment due to human use - present knowledge and future challenges. *Journal of Environmental Management*, *90*(8), 2354–2366. doi:10.1016/j.jenvman.2009.01.023

Le-Minh, N., Khan, S. J., Drewes, J. E., & Stuetz, R. M. (2010). Fate of antibiotics during municipal water recycling treatment processes. *Water Research*, *44*(15), 4295–4323. doi:10.1016/j.watres.2010.06.020

Li, Jianan, Cheng, Weixiao, Xu, Like, Jiao, Yanan, Ali Baig, Shams, C. H. (2015). Occurrence and removal of antibiotics and the corresponding resistance genes in wastewater treatment plants: effluents' influence to downstream water environment. *Environmental Science Pollution Research*, *318*, 319–328. doi:10.1016/j.jhazmat.2016.07.021

Li, C., Chen, J., Wang, J., Ma, Z., Han, P., Luan, Y., & Lu, A. (2015). Occurrence of antibiotics in soils and manures from greenhouse vegetable production bases of Beijing, China and an associated risk assessment. *Science of the Total Environment*, *521–522*, 101–107. doi:10.1016/j.scitotenv.2015.03.070

Liu, S., Zhao, X. rong, Sun, H. yuan, Li, R. ping, Fang, Y. feng, & Huang, Y. ping. (2013). The degradation of tetracycline in a photo-electro-Fenton system. *Chemical Engineering Journal*, *231*, 441–448. doi:10.1016/j.cej.2013.07.057

Magdaleno, A., Juárez, Á. B., Paz, M., Tornello, C., Núñez, L., & Moretton, J. (2012). Ecotoxicological and genotoxic evaluation of hospital wastewaters. *Acta Toxicol{ó}gica Argentina*, *20*(1), 14–24. Recuperado de

Martínez-Carballo, E., González-Barreiro, C., Scharf, S., & Gans, O. (2007). Environmental monitoring study of selected veterinary antibiotics in animal manure and soils in Austria. *Environmental Pollution*, *148*(2), 570–579. doi:10.1016/j.envpol.2006.11.035

Marx, C., Günther, N., Schubert, S., Oertel, R., Ahnert, M., Krebs, P., & Kuehn, V. (2015). Mass flow of antibiotics in a wastewater treatment plant focusing on removal variations due to operational parameters. *Science of the Total Environment*, *538*, 779–788. doi:10.1016/j.scitotenv.2015.08.112

Molla, W., Frankena, K., Gari, G., & de Jong, M. C. M. (2017). Field study on the use of vaccination to control the occurrence of lumpy skin disease in Ethiopian cattle. *Preventive Veterinary Medicine*, *147*, 34–41. doi:10.1016/j.prevetmed.2017.08.019

Mudryk, J., Skórczewski, P., Mudryk, Z. J., Jankowska, M., Perli, P., & Zdanowicz, M. (2013). Antibiotic resistance of neustonic and planktonic fecal coliform bacteria isolated from two water basins differing in the level of pollution Resistencia a antibióticos de bacterias coliformes fecales , nesutónicas y planctónicas , aisladas de dos cuerpos, *23*(3), 431–439.

Murphy, E. A., Post, G. B., Buckley, B. T., Lippincott, R. L., & Robson, M. G. (2012). Future Challenges to Protecting Public Health from Drinking-Water Contaminants. *Annual Review of Public Health*, *33*(1), 209–224. doi:10.1146/annurev-publhealth-031811-124506

Nieto, A., Borrull, F., Marcé, R. M., & Pocurull, E. (2007). Selective extraction of sulfonamides, macrolides and other pharmaceuticals from sewage sludge by pressurized liquid extraction. *Journal of Chromatography A*, *1174*(1–2), 125–131. doi:10.1016/j.chroma.2007.09.068

Nnadozie, C. F., Kumari, S., & Bux, F. (2017). Status of pathogens, antibiotic resistance genes and antibiotic residues in wastewater treatment systems. *Reviews in Environmental Science and Biotechnology*, *16*(3), 1–25. doi:10.1007/s11157-017-9438-x

OMS. (2016). OMS | Uso de los antimicrobianos. *WHO*. Recuperado de

OMS. (2017). OMS | Las 10 principales causas de defunción. Recuperado de

Organización Panamericana de la Salud. (2015). Plan de acción sobre la resistencia a los antimicrobianos antimicrobianos, 1–3.

Özcan, A., Özcan, A., & Demirci, Y. (2016). Evaluation of mineralization kinetics and pathway of norfloxacin removal from water by electro-Fenton treatment. *Chemical Engineering Journal*, *304*, 518–526. doi:10.1016/j.cej.2016.06.105

Padilla-Robles, B. G., Alonso, A., Martínez-Delgadillo, S. A., González-Brambila, M., Jaúregui-Haza, U. J., & Ramírez-Muñoz, J. (2015). Electrochemical degradation of amoxicillin in aqueous media. *Chemical Engineering and Processing: Process Intensification*, *94*, 93–98. doi:10.1016/j.cep.2014.12.007

Pan, M., & Chu, L. M. (2017). Fate of antibiotics in soil and their uptake by edible crops. *Science of the Total Environment*. doi:10.1016/j.scitotenv.2017.04.214

Pan, M., & Chu, L. M. (2017). Leaching behavior of veterinary antibiotics in animal manure-applied soils. *Science of the Total Environment*, *579*, 466–473. doi:10.1016/j.scitotenv.2016.11.072

Pan, M., & Chu, L. M. (2017). Leaching behavior of veterinary antibiotics in animal manure-applied soils. *Science of the Total Environment*, *579*, 466–473. doi:10.1016/j.scitotenv.2016.11.072

Peña-Álvarez, A., & Castillo-Alanís, A. (2015). Identificación y cuantificación de contaminantes emergentes en aguas residuales por microextracción en fase sólida-cromatografía de gases-espectrometría de masas (MEFS-CG-EM). *Tip*, *18*(1), 29–42.doi:10.1016/j.recqb.2015.05.003

Poel, I. Van De. (2003). The transformation of technological regimes. *Research Policy*, *32*(1), 49–68. doi:10.1016/S0048-7333(01)00195-0

Reynaud, S., & Deschaux, P. (2006). The effects of polycyclic aromatic hydrocarbons on the immune system of fish: A review. *Aquatic Toxicology*, *77*(2), 229–238. doi:10.1016/j.aquatox.2005.10.018

Rizzo, L., Manaia, C., Merlin, C., Schwartz, T., Dagot, C., Ploy, M. C. ., Fatta-Kassinos, D. (2013). Urban wastewater treatment plants as hotspots for antibiotic resistant bacteria and genes spread into the environment: A review. *Science of the Total Environment*, *447*, 345–360. doi:10.1016/j.scitotenv.2013.01.032

Santos, L., & Ramos, F. (2016). Analytical strategies for the detection and quantification of antibiotic residues in aquaculture fishes: A review. *Trends in Food Science and Technology*, *52*, 16–30. doi:10.1016/j.tifs.2016.03.015

Sapkota, A., Sapkota, A. R., Kucharski, M., Burke, J., McKenzie, S., Walker, P., & Lawrence, R. (2008). Aquaculture practices and potential human health risks: Current knowledge and future priorities. *Environment International*, *34*(8), 1215–1226.doi:10.1016/j.envint.2008.04.009

Shi, W., Yue, T., Du, Z., Wang, Z., & Li, X. (2016). Surface modeling of soil antibiotics. *The Science of the Total Environment*, *543*(Pt A), 609–19. doi:10.1016/j.scitotenv.2015.11.077

Singer, A. C., Järhult, J. D., Grabic, R., Khan, G. A., Lindberg, R. H., Fedorova, G., … Söderström, H. (2014). Intra- and inter-pandemic variations of antiviral, antibiotics and decongestants in wastewater treatment plants and receiving rivers. *PLoS ONE*, *9*(9).doi:10.1371/journal.pone.0108621

Sui, Q., Cao, X., Lu, S., Zhao, W., Qiu, Z., & Yu, G. (2015). Occurrence, sources and fate of pharmaceuticals and personal care products in the groundwater: A review. *Emerging Contaminants*, *1*(1), 14–24. doi:10.1016/j.emcon.2015.07.001

Tasho, R. P., & Cho, J. Y. (2016). Science of the Total Environment Veterinary antibiotics in animal waste , its distribution in soil and uptake by plants : A review. *Science of the Total Environment*, *563–564*(3), 366–376. doi:10.1016/j.scitotenv.2016.04.140

Ternes, T. A., Prasse, C., Eversloh, C. L., Knopp, G., Cornel, P., Schulte-Oehlmann, U., Oehlmann, J. (2017). Integrated Evaluation Concept to Assess the Efficacy of Advanced Wastewater Treatment Processes for the Elimination of Micropollutants and Pathogens. *Environmental Science and Technology*, *51*(1), 308–319. doi:10.1021/acs.est.6b04855

Ternes, T., Joss, A., & 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*, 1–2. doi:10.1016/j.watres.2015.02.055

Underwood, J. C., Harvey, R. W., Metge, D. W., Repert, D. A., Baumgartner, L. K., Smith, R. L.,Barber, L. B. (2011). Effects of the antimicrobial sulfamethoxazole on groundwater bacterial enrichment. *Environmental Science and Technology*, *45*(7), 3096–3101. doi:10.1021/es103605e

Van Boeckel, T. P., Brower, C., Gilbert, M., Grenfell, B. T., Levin, S. A., Robinson, T. P., Laxminarayan, R. (2015). Global trends in antimicrobial use in food animals. *Proceedings of the National Academy of Sciences*, *112*(18), 5649–5654. doi:10.1073/pnas.1503141112

van Dijk, L., Hayton, A., Main, D. C. J., Booth, A., King, A., Barrett, D. C., Reyher, K. K. (2017). Participatory Policy Making by Dairy Producers to Reduce Anti-Microbial use on Farms. *Zoonoses and Public Health*, *64*(6), 476–484. doi:10.1111/zph.12329

Verlicchi, P., Al Aukidy, M., & Zambello, E. (2012). Occurrence of pharmaceutical compounds in urban wastewater: Removal, mass load and environmental risk after a secondary treatment-A review. *Science of the Total Environment*, *429*, 123–155. doi:10.1016/j.scitotenv.2012.04.028

Villalobos, A. P., Barrero, L. I., Rivera, S. M., Ovalle, M. V., & Valera, D. (2013). Vigilancia de infecciones asociadas a la atención en salud, resistencia bacteriana y consumo de antibióticos en hospitales de alta complejidad, Colombia, 2011. *Biomédica*, *34*(0), 67. doi:10.7705/biomedica.v34i0.1698

Vo, T. D. H., Bui, X. T., Cao, N. D. T., Luu, V. P., Nguyen, T. T., Dang, B. T., … Dao, T. S. (2016). Investigation of antibiotics in health care wastewater in Ho Chi Minh City, Vietnam. *Environmental Monitoring and Assessment*, *188*(12). doi:10.1007/s10661-016-5704-6

von Schiller, D., Acuña, V., Aristi, I., Arroita, M., Basaguren, A., Bellin, A., … Elosegi, A. (2017). River ecosystem processes: A synthesis of approaches, criteria of use and sensitivity to environmental stressors. *Science of the Total Environment*, *596–597*(April), 465–480. doi:10.1016/j.scitotenv.2017.04.081

Werbeloff, L., Brown, R. R., & Loorbach, D. (2016). Pathways of system transformation: Strategic agency to support regime change. *Environmental Science and Policy*, *66*, 119–128. doi:10.1016/j.envsci.2016.08.010

Zhang, Q., & Dick, W. A. (2014). Growth of soil bacteria, on penicillin and neomycin, not previously exposed to these antibiotics. *Science of the Total Environment*, *493*, 445–453. doi:10.1016/j.scitotenv.2014.05.114

Zhang, Q. Q., Ying, G. G., Pan, C. G., Liu, Y. S., & Zhao, J. L. (2015). Comprehensive evaluation of antibiotics emission and fate in the river basins of China: Source analysis, multimedia modeling, and linkage to bacterial resistance. *Environmental Science and Technology*, *49*(11), 6772–6782. doi:10.1021/acs.est.5b00729

Zhang, W., Naveena, B. M., Jo, C., Sakata, R., Zhou, G., Banerjee, R., & Nishiumi, T. (2017). Technological demands of meat processing–An Asian perspective. *Meat Science*, *132*, 35–44. doi:10.1016/j.meatsci.2017.05.008