PHARMACEUTICAL WASTE MANAGEMENT: A REVIEW

Article · November 2016

CITATIONS
8

READS
13,936

3 authors, including:

Yamini Shah
LMCollege of Pharmacy
22 PUBLICATIONS **171** CITATIONS

SEE PROFILE

EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 3
Issue: 12
192-206
Year: 2016

PHARMACEUTICAL WASTE MANAGEMENT: A REVIEW

Susmita Rajbongshi[1]*, Yamini Dushyant Shah[2] and Ahsan Ullah Sajib[3]

[1]*Student Bachelor of Pharmacy, LM College of Pharmacy (LMCP), Navarangpura - 380009, Ahmedabad, Gujarat Technological University, Gujarat, India.
[2]Dr. and Associate Professor, Department of Pharmaceutics and Pharmaceutical Technology, LM College of Pharmacy, Navarangpura - 380009, Ahmedabad, Gujarat Technological University, Gujarat, India.
[3]Officer, Production Incepta Pharmaceuticals Ltd, Dhaka - 1207, B. Pharm (LMCP), M. Pharm, North South University (NSU), Dhaka, Bangladesh.

***Corresponding Author: Susmita Rajbongshi**
Student Bachelor of Pharmacy, LM College of Pharmacy (LMCP), Navarangpura - 380009, Ahmedabad, Gujarat Technological University, Gujarat, India.

Article Received on 03/10/2016 **Article Revised on 23/10/2016** **Article Accepted on 13/11/2016**

ABSTRACT
Increasing environmental pollution coupled with the increasing amount of uncontrollable pharmaceutical waste entering the eco-system, has attracted the attention of policy makers to focus on the research to mitigate harmful emissions and also spearhead management of pharmaceutical waste. This paper focuses on how pharmaceutical waste can be handled, generated, disposed, and how regulations and strategies can be reinforced step by step. This review shows that if all sub areas of pharmaceutical waste management can efficiently work back to back environmental pollution and dangers to human health can reduce significantly.

KEYWORDS: Pharmaceutical Waste Environmental pollution Waste Management Human health Pharmaceutical and Personal Care Products (PPCPs).

1. INTRODUCTION
"Pharmaceutical waste includes expired, unused, spilt, and contaminated pharmaceutical products, drugs, vaccines and sera that are no longer required and need to be disposed of appropriately. The category also includes discarded items used in the handling of pharmaceuticals, such as bottles or boxes with residues, gloves, masks, connecting tubing and drug vials.[1] Generally, there are two major categories of pharmaceutical waste as depicted from pharmaceutical management point of view namely; pharmaceutical waste that include expired or not used drugs consisting of syringes and vials that are disposed by domestic households and health care treatment industries and those pharmaceutical waste generated from hospitals and health care and research organisation.[2,3] Ideally, Pharmaceuticals are discarded and treated by high temperature (i.e. above 1,200ºC) incineration. Equipment used in such type of disposal method of high temperature incineration coupled with enough emission controls mainly exist in developed countries.[1] Polyvinyl chloride (PVC) plastic however must not be burnt in the process of incineration. PVC wastes reduce the life span of the incinerator and produce harmful pollutants to the environment such as hazardous HCl gas, dioxans, furan, etc. Among other things PVC plastic create challenges in the process of plastic recycling and is also responsible for the reduction in plastic recycling ratio by generating compounds or worsening the nature of other plastic materials.[4] In 1994, the United States Environmental Protection Agency (EPA) discovered that the emissions produced from health care incinerators were responsible for high levels of pollutants such as dioxan and furan in the environment.[5]

2. LITERATURE REVIEW
2.1 Sources of Pharmaceutical Waste
Most of the published articles concerning pharmaceuticals for human use have mainly focused on aquatic systems, in which effluent is generally considered as the major source of emission to the environment through its discharge of pharmaceuticals either in its natural form or as metabolites.[1] Generally, waste water-treatment plants (WWTPs) do not fully remove pharmaceuticals due to lack of proper design.[6,7,8,9] Veterinary use pharmaceuticals are regularly discharged into the environment by means of either direct human and animal excretion (through urine and dung from grass-feeding animals) or by way of manure application on agricultural soils.[6,10,11,12] A well-known source for pharmaceuticals and personal care products (PPCPs) enter the environment through effluent from waste water treatment plants (WWTP).[13] Other ways in which PPCPs enter into the aquatic systems is through leakages from underground sewage systems. Combined sewer overflows (CSOs) are used to transfer

storm water runoff in many urban areas and this creates contamination of raw sewage (with quantities of PPCPs) and storm water into stream ecosystems.[13,14,15] Pharmaceutical manufacturing industries are a major source of PPCPs into the aquatic environment.[16,17,18] The New York City Department of Environmental Protection in 2010 calculated the existence of PPCPs in the city's water supply sources and found 14 of 72 targeted compounds.[19] Other ways in which personal care products enter into the aquatic ecosystem is through human entertainment and recreational activities such as showering, bathing, swimming and other modern processes.[20, 17]

2.2 Occurrence/ generation of pharmaceutical waste

Varieties of pharmaceutical products are traced in the aquatic resources and soil such as analgesics, antibiotic and stimulants. According to Environmental Protection Authority Victoria,[21] a point source is a single, identifiable source of pollution such as a pipe or a drain. Industrial wastes are commonly discharged to rivers and the sea in this way. High risk point source waste discharges are regulated by EPA through the works approval and licensing system and associated compliance and enforcement activities. Non-point sources of pollution are often termed 'diffuse' pollution and refer to those inputs and impacts which occur over a wide area and are not easily attributed to a single source. They are often associated with particular land uses, as opposed to individual point source discharges. According to European Environmental Agency,[22] diffuse pollution can be caused by a variety of activities that have no specific point of discharge. Agriculture is a key source of diffuse pollution, but urban land, forestry, atmospheric deposition and rural dwellings can also be important sources. Point source and diffuse source are significant pathways in which pharmaceuticals are discharged into the environment.[19] Recently a wide range of pharmaceutical products or metabolites have been discovered in in various aquatic environments and published in literature.[23, 24]

Table 1: Sources and Occurrences of Pharmaceutical Waste

Sr.	Compounds	Sources	Concentrations	Method of Extraction	Source Type	References
	Hormone					
	Antibiotics					
1	Tylosin	Umgeni River water system, KwaZulu-Natal, South Africa	0.21– 21.99 µg/L	Solid-phase extraction Hydrophilic–lipophilic balance (HLB)	Diffuse Source	[69]
		Arkansas streams, USA	0.06 and 0.18 µg/L	Solid-phase extraction (SPE)/ Concentration measured by gas chromatography (GC) and mass spectrometry (MS)	Diffuse Source	[70]
2	Streptomycin	Umgeni River water system, KwaZulu-Natal, South Africa	0.81– 8.42 µg/L	Solid-phase extraction Hydrophilic–lipophilic balance (HLB)	Diffuse Source	[69]
3	Sulfamethoxazole	Umgeni River water system, KwaZulu-Natal, South Africa	3.68 µg/L	Solid-phase extraction Hydrophilic–lipophilic balance (HLB)	Diffuse Source	[69]
		USA drinking water between 2006 and 2007	12 ng/L	Solid phase extraction (SPE)/ Analysed by Chromatography or gas chromatography with tandem mass spectrometry (LC MS/MS and GC-MS/MS	Point Source	[71]
		River and sewage water	0.33– 0.61 µg/L	Mixed hemimicelles solid-phase extraction/ liquid chromatography–spectrophotometry	Diffuse Source	[46]
		Effluents arising from WWTPs in Scotland	7 ng L−1	HPLC-MS/MS system	Point Source	[49]
4	Nalidixic acid	Umgeni River water system, KwaZulu-Natal, South Africa	1.73–30.84 µg/L	Solid-phase extraction Hydrophilic–lipophilic balance (HLB)	Diffuse Source	[69]
		Hospital effluent, wastewater treatment plant influent and effluent and in surface water in Australia	0.75 µg/L	Oasis HLB 200/500 mg SPE cartridges. Extraction done using vacuum extraction manifold	Point Source	[72]
5	Ampicillin	Umgeni River water system, KwaZulu-Natal, South Africa	2.52 to 14.48 µg/L	Solid-phase extraction Hydrophilic–lipophilic balance (HLB)	Diffuse Source	[69]
		Industrial and wastewater treatment	2.2–25.6 µg/L	Mixed mode solid phase extraction using liquid chromatography with UV-	Point Source	[73]

		samples		DAD detection		
6	Erythromycin	Umgeni River water system, KwaZulu-Natal, South Africa	0.58 - 22.57 µg/L	Solid-phase extraction Hydrophilic–lipophilic balance (HLB)	Diffuse Source	[69]
		Wastewater effluents in Germany	6.0 µg/L	Extraction was performed using lyophilization or solid phase extraction followed by HPLC-electrospray-MS/MS detection.	Point Source	[74]
7	Tetracycline	Umgeni River water system, KwaZulu-Natal, South Africa	0.64 - 5.68 µg/L	Solid-phase extraction Hydrophilic–lipophilic balance (HLB)	Diffuse Source	[69]
		Waste water and surface water of China	>1 mg/L waste water >0.25 mg/L in surface water	Liquid chromatography-electrospray ionization mass spectrometry	Diffuse Source	[75]
8	Ciprofloxacin	Umgeni River water system, KwaZulu-Natal, South Africa	0.71 µg/L - 16.9 µg/L.	Solid-phase extraction Hydrophilic–lipophilic balance (HLB)	Diffuse Source	[69]
		Pharmaceutical industries wastewater treatment plant samples in Sweden	28–31 mg/L	Surveyor HPLC and LCQ-Duo MS (ThermoFinnigan Inc., USA) acquiring MS/MS data in ESI+ mode.	Point Source	[17]
9	Chloramphenicol	Umgeni River water system, KwaZulu-Natal, South Africa	0.5–10.7 µg/L	Solid-phase extraction Hydrophilic–lipophilic balance (HLB)	Diffuse Source	[69]
		Industrial and sewage treatment plant Wastewaters in Germany	4.0– 10 µg/L	Extraction was performed using lyophilization or solid phase extraction followed by HPLC-electrospray-MS/MS detection.	Point Source	[74]
	Lipid regulator					
10	Bezafibrate	Umgeni River water system, KwaZulu-Natal, South Africa	0.81–8.71 µg/L	Solid-phase extraction Hydrophilic–lipophilic balance (HLB)	Diffuse Source	[69]
		Sewage treatment plants and in receiving water in Finland	0.42 µg/L	Solid-phase extraction (SPE)/ HPLC-ESI-MS/MS	Point Source	[69]

(Continued on next page)

Table 1 (Continued)

Compounds / **Hormone**	**Sources**	**Concentrations**	**Method of Extraction**	**Source Type**	**References**
11 Gemfibrozil	Wastewater treatment	56–1,032 ng/L	Solid-phase extraction (SPE)/ LC-MS/MS	Point	[26]

		plants (WWTPs) Rome (Italy)			Source	
	β-blocker					
12	Atenolol	Umgeni River water system, KwaZulu-Natal, South Africa	0.96–39.10 µg/L	Solid-phase extraction Hydrophilic–lipophilic balance (HLB)	Diffuse Source	[69]
	Antipyretics					
13	Ibuprofen	Umgeni River water system, KwaZulu-Natal, South Africa	0.8– 18.9 µg/L	Solid-phase extraction Hydrophilic–lipophilic balance (HLB)	Diffuse Source	[69]
		Drinking and reclaimed wastewater in France	0.51–1.35 µg/L	MCX Oasis cartridges (Waters, Saint Quentin en Yvelines, France) (water samples eluted at flow rate: 12-18 mL.min-1)	Point Source	[77]
		Waste water in California, USA	3.23–25.8 µg/L	Sulfonated polystyrene divinylbenzene solid phase extraction disks (3M Empore SDB-RPS).	Point Source	[78]
		Raw and treated wastewater in Spain	2.3–10.4 µg/L	Solid-phase extraction and liquid chromatography– tandem mass spectrometry.	Point Source	[79]
		Wastewater treatment plants (WWTPs) Rome (Italy)	41–184 ng/L	Solid-phase extraction (SPE)/ LC-MS/MS	Point Source	[26]
14	Ketoprofen	Umgeni River water system, KwaZulu-Natal, South Africa	0.4–8.2 µg/L	Solid-phase extraction Hydrophilic–lipophilic balance (HLB)	Diffuse Source	[69]
		Raw and treated wastewater in Spain	0.14–0.35 µg/L	Solid-phase extraction and liquid chromatography– tandem mass spectrometry.	Point Source	[79]
15	Diclofenac	Umgeni River water system, KwaZulu-Natal, South Africa	1.1–15.6 µg/L	Solid-phase extraction Hydrophilic–lipophilic balance (HLB)	Diffuse Source	[69]
		Raw and treated wastewater in Spain	0.48–0.76 µg/L	Solid-phase extraction and liquid chromatography– tandem mass spectrometry.	Point Source	[79]
		Effluents arising from WWTPs in Scotland	24.2 - 927 ng L−1	HPLC-MS/MS system	Point Source	[49]
		Wastewater treatment plants (WWTPs) Rome (Italy)	321–1,424 ng/L	Solid-phase extraction (SPE)/ LC-MS/MS	Point Source	[26]
16	Aspirin	Umgeni River water system, KwaZulu-Natal, South Africa	2.2–10.0 µg/L	Solid-phase extraction Hydrophilic–lipophilic balance (HLB)	Diffuse Source	[69]
		Raw and treated	2.2–6.1 µg/L	Solid-phase extraction and liquid	Point	[79]

		wastewater in Spain		chromatography– tandem mass spectrometry.	Source	
17	Acetaminophen	Umgeni River water system, KwaZulu-Natal, South Africa	5.8–58.7 µg/L	Solid-phase extraction Hydrophilic–lipophilic balance (HLB)	Diffuse Source	[69]
		wastewater influents in France	11.3 µg/L	MCX Oasis cartridges (Waters, Saint Quentin en Yvelines, France) (water samples eluted at flow rate: 12-18 mL.min-1)	Point Source	[77]
		Surface water in France	10.6– 68.1 ng/L	MCX Oasis cartridges (Waters, Saint Quentin en Yvelines, France) (water samples eluted at flow rate: 12-18 mL.min-1)	Diffuse Source	[77]
	Anticonvulsants					
18	carbamazepine	Wastewater treatment plants (WWTPs) Rome (Italy)	69–886 ng/L	Solid-phase extraction (SPE)/ LC-MS/MS	Point Source	[26]

Table[1] shows some of the pharmaceutical waste detected in different places around the world. The table also shows their concentrations and it is clear that the world environment is at high risk arising from pharmaceutical waste pollution.

Pharmaceuticals are one of the most significant emerging categories of environmental pollutants. Their existence has been found in wastewater, natural waters, effluents, sludge and sediments. Recent findings show their existence in samples taken from different countries around the globe.[25] For example; the existence of 12 pharmaceuticals, not to mention 3 steroid hormones, in 4 WWTPs found in the most crowded Italian city, Rome, has been discovered in concentrations levels in waters of Rivers Aniene and Tiber. The discovery shows that the conventional method of wastewater treatment does not efficiently eliminate pharmaceuticals targeted for removal which resulted in the presence of a wide range of quantified pharmaceuticals in effluents when sampled in both seasons (spring and winter). As a consequence, the discovery found contamination in the receiving waters.[26] In a review a total of ninety three pharmaceuticals have been found to exist in the surface water of USA, the highly concentrated common occurrence being the antibiotic type a total of (Twenty Seven) and antidepressant (total of Fifteen).[27] The study of emerging organic contaminants in Umgeni River water system, KwaZulu-Natal, South Africa found the existence of seventeen pharmaceuticals nine antibiotics, five antipyretics, one β-blocker, one lipid regulator and a psychostimulant in wastewater from a domestic wastewater treatment plant. All the compounds were found in the wastewater at high concentrations but similar to those obtained from other countries in Europe and Asia.[28] In some research on wastewater, surface water and groundwater of Nairobi and Kisumu city, Kenya found the occurrence of twenty four pharmaceuticals. The most commonly occurring compounds found were antiretrovirals, nevirapine, zidovudine, antibiotics, metronidazole, sulfamethoxazole and trimethoprim. Those with high concentration values up to 160 mg/L compounds were for example; paracetamol in wastewater and lamivudine in river water, were detected.[29] In some research it was found that Landfill leachates if not treated properly could result in groundwater pollution due to the presence of pharmaceuticals.[30]

2.3 Handling / Removal

Among other treatment processes used to neutralize and remove Pharmaceutical and personal care products (PPCPs), activated sludge system is the most common treatment method. This conventional water and effluent treatment method does not efficiently remove PPCPs. This treatment process for removing PPCPs is also faced with a lot of challenges including the composition of PPCPs, environmental conditions, pre-treatment system, operational conditions as well as microbial community existing in activated sludge system. As a result the method of treating PPCPs needs to be improved to mitigate the demand of treating PPCPs that contains wastewater.[31] Incineration equipment, that are incorporated with controlled emission systems are mainly available in developed countries.[1] For example; one study suggests that environmental pollution and associated risk in usage of pharmaceuticals maybe higher in developing countries than in developed and industrialised countries.[32]

2.4 Risk of Pharmaceutical Waste

Water recycling may increase in the years to come for instance in the United States of America, the population growth and not to mention droughts caused by climate change coupled with the increase in PPCPs in the aquatic environment could result in increased concentrations of PPCPs, antibiotic resistance bacteria (ARB) and antibiotic resistance genes (ARG) in effluents. Consequently, this entails additional research as inevitable as well as improvements in waste water treatment methods in order to keep a healthy and sound ecosystem and enhance sustainability of the world water supply system.[33] A study suggests that the environmental risk regarding the usage and emission of pharmaceuticals into the ecosystem in developing countries may be more than that of the developed world.[34,32] Pharmaceutical waste products in water become a mixture of various heavy metals and organic pathogens that are likely to have potential mutagenic and genotoxic effect when living organisms are exposed to it.[35] Some studies have revealed that people residing near pharmaceutical industries have been infected with water borne diseases which are caused by contamination of water. These diseases caused by pharmaceuticals in water include hypertension, gastroenteritis, cardiac troubles, fetomaternal death, diabetes mellitus and impaired neurobehavioral effects. All these diseases have been attributed to pollution caused by pharmaceutical industrial effluents which generate toxic waste that are a blend of inorganic and organic pollutants.[35] All forms of pharmaceutical waste in either aquatic or terrestrial life can be polluted by these pharmaceutical compounds that are significantly toxic in nature and their presence in concentration. Pharmaceuticals generally contain lipophilic and non-biodegradable existence and an incorporated biological activity that makes it a matter of concern to our environmental system.[36,35] Pharmaceutical industry may inject pollutants into the ecosystem. These pollutants include heavy metals such as cadmium (Cd), lead (Pb), chromium (Cr), nickel (Ni) and mercury (Hg), in addition to toxic agents which are organic in nature or phenolic compounds. These compounds pollute the surface and ground waters. The nature of these heavy metals (i.e. mutagenic and carcinogenic) has become the main focus of study when dealing with the ecosystem and not to mention the food chain.[37,35] Strong evidence from literature concerning health and environmental adverse effects of commonly occurring contaminants on humans has so far yielded very little information and the worse has been the

understanding of the effects posed by exposure of human beings to these multifaceted combinations arising from these modulators.[20,38,39,40]

World Health Organization and United Nations Environmental Programme report of 2013 reveals that many countries including developing ones are on the threat of imminent health risks which is likely to be complicated and challenging because of the existence of pharmaceutically active agents in aquatic system.[20, 41]

2.5 Disposal/ Treatment of Pharmaceutical Waste

In as much as thermal treatment such as incineration is applied to all kinds of medical waste (MW) other than infectious ones, this treatment technology is generally expensive than the conventional disinfection method. However, it still remains the top used method of medical waste treatment in less developed countries. The challenging issues regarding incineration are the disposal of ash and the treatment of gaseous pollutants containing furans, dioxins and mercury. In addition, incineration has the advantage of reducing the volume size by 90% of the treated products. Other thermal technologies that have hardly been used to medical waste treatment include gasification, pyrolysis and plasma treatment method.[42] Pharmaceutical waste sludge in some studies was used for making bricks for construction purposes. It was found that 10% of the sludge in the brick product achieved significant compressive strength properties. The use of this method is highly economical due to the fact that the use of readily available industrial sludge greatly reduces the cost of end products in relation to the traditional raw materials and greatly reduces the exploitation of the conventional raw materials.[43] Unlawful disposal of not used pharmaceuticals has been found to be a great concern in many developed countries.[44, 45, 46] Unlawful disposal of medicines could be reduced by educating the public about safe and proper disposal of medicines and also making easy access to take-back strategies.[44, 47, 46] In view of PPCPs flowing virtually untreated through the modern sewage treatment system reveals the inadequacy of the current methods of pharmaceutical waste and sewage treatment to process and remove PPCPs.[48] Insufficient removal of pharmaceuticals compounds when treating wastewater results in contamination into the environmental water systems. The flow of pharmaceuticals into wastewater treatment plants (WWTPs) effluents into lakes, rivers and oceans has resulted into highly traceable concentrations of pharmaceuticals in the waters around the world.[49] There are several disposal methods for bio solids formed during the process of water treatment which includes incineration, land application of dewatered solids for fertilizer and landfills. The last two techniques may result in the contamination of PPCPs to ecosystem waters.[13]

2.6 Policies and Strategies for removal and treatment of Pharmaceutical Waste

Some studies have argued categorically that educational programmes could be treated as the best approach for protecting human health and ecosystem from the negative effects of pharmaceutical waste (PW). In view of such development it is advised that training-of-trainee programmes of Pharmaceutical Waste Management (PWM) be introduced and established for every healthcare staff in hospitals during commencement of employment and continued regular teachings through workshops.[50] When comparing the data from the ERA procedures of the US FDA, EU EMEA, and Japan, there is much inconsistency in their environmental risk assessment strategies for pharmaceutical waste management. The inferences when compared do not agree. As a result, the ecological impacts described relating the occurrence of PPCPs in the ecosystem will be inadequate. In general, the US and EU methods produce results that vaguely agree, but the Japanese methods produce outcomes in contradictory interpretations of the impact of Sulfamethoxazole (SMZ) on the environment.[32,33] It is argued that policy solutions can never be treated as universal. This is due to the fact that particular market orientations and populations are inconsistent. For example, the main issues faced by industrialised countries are that there are unable to change their systems and the challenges of balancing the interests of industry, health professions as well as the state. On the contrary less developed countries need to build an infrastructure for the procurement, quality and storage as well as distribution of medicines. As such if pharmaceutical policy is considered non – universal it would benefit policy makers if they realize and develop such similar approach. In our current environment, important drugs lists are a tool to enhance the system and channel resources to infrastructure building. On the contrary developed countries already have the needed infrastructure in place and more funds to procure medicines.[51] Based on the pharmaceuticals abatement strategies highlighted in one review by Benjamin D. Blair, no ideal solution currently exists for the complete prevention of this complex class of pollutants from entering the aquatic environment. The impacts environmental and the occurrence of pharmaceuticals in water sources meant for drinking has led policy makers to adapt solutions to these challenges, yet a systematic study evaluating the key strategies is still missing.[52] Stakeholders from academia, government and the pharmaceutical and consulting industries from Canada, the United States and Europe had contradicting suggestions on the science and management of pharmaceuticals in ecosystem, even if some acceptable trends and tendencies have been observed.[53] Until now there are no international standards for the proper analysis of the impact of pharmaceuticals in aquatic environment.[23] Due to increasing concerns across the globe, the International Society of Doctors for the Environment has come up with the theme of "Environmentally persistent pharmaceutical pollutants"

as an Emerging Policy Issue under the Strategic Approach to International Chemicals Management.[19] Recently there has been an increase in the growth of organic pollutants in the ecosystem as a result of unlawful disposal of pharmaceuticals done due to lack of stringent regulatory measures not put in place or not been followed according to the existing laws under environmental protection laws.[20, 54, 55, 56, 57] Recently a number of different types of pharmaceutical contaminants have been detected in water samples around the globe namely in USA, China, Germany, Canada, Brazil, Holland, including South Africa partly due to failure of standardized allowable discharge limits.[20, 58, 59, 60, 61]

2.7 Methodical ways to Neutralise Pharmaceutical Waste

A variety of new technologies for treating and neutralizing pharmaceuticals from wastewaters has been developed. These technologies have a promising future and adequately improve the removal rate of pharmaceuticals from effluents. These technologies include Advanced Oxidation Processes (AOPs), ozonation, direct photolysis, oxidation, TiO2 photocatalysis, Fenton reactions, solar photocatalysis and ultrasonic irradiation. Relating these technologies to each other is so much problematic. Therefore, further research is needed in this category of study to enhance treatment efficiencies and also to determine compounds that degrade as well as its associated cost and feasibility of the whole applications.[62] Due to the impact on the ecosystem and high cost of disposing medical waste by incineration method has prompted many researchers and firms to work on developing other means of treatment methods for infectious medical wastes. The current known replacement for incineration is autoclaving method. This method employs treatment of infectious waste by adding dry heat or steam to increase the temperature of infectious waste to values sufficient enough to eliminate any microbial contamination. Such system mainly works at temperatures ranging from 121 to 163^{o}C.[63,64] The advantageous part of autoclave treatment process is that after waste treatment the remaining waste can be disposed at the municipal solid waste (MSW) landfill site in the same way as non-infectious waste.[63,65] Other advantage of autoclave treatment method of infectious medical waste over incineration is that it does not produce pollutants generated from PVC and other products such as mercury, furan and dioxin that are emitted into the environment during incineration.[63, 64] There are also disadvantage in the use of autoclaving as an infectious waste treatment technology. Autoclave process has heat waste through steam to eliminate the pathogens without direct burning the waste and keeping its appearance like before, the resultant waste after treatment does not distinguishes itself from untreated infectious waste hence giving the perception that untreated infectious waste is being dumped on landfill sites.[63,65] Due to this fact autoclaved waste is often pre-treated through incineration before final disposal due to the reluctance of many communities to allow non-incinerated infectious waste into their landfills, making the autoclave treatment unreliable.[1] Even if concentrations of pharmaceutical and personal care products PPCPs in the ecosystem are less, continuous exposure to these chemicals becomes a major issue which has unknown complications in the long run. As a result PPCPs removal and neutralization became a focal point of many studies. There are generally three categories of neutralizing and removing PPCPs namely, physical, biological and chemical methods. Waste water treatment plant is one of the most common methodical ways of neutralizing pharmaceutical waste because all the unprocessed pharmaceutical waste from other treatment technologies ends up in aquatic environment at the end of the day. Table (2) shows the removal efficiency of PPCPs by Waste Water Treatment Plant (WWTPs) and also quantifies the percentage of removal for each treatment process.[31]

Table 2: The removal efficiency of PPCPs by WWTPs.[31]

Sr.	Compounds	Initial concentration	Treatment processes	Removal efficiency (%)	References
	Hormone				
1	Estriol	60 ng/l	Grit channels + primary clarifies + conventional activated sludge	66.8	Blair et al., 2015
2	Estrone	57 ng/l		93.7	Blair et al., 2015
	Antibiotics				
3	Sulfamethoxazole	7400 ng/l	Grit channels + primary clarifies + conventional activated sludge	_35.8	Blair et al., 2015
		10 mg/kg dry weight sludge	Anaerobic sludge digestion	100	Narumiya et al., 2013
4	Sulfadiazine	20 ng/l	Grit channels + primary clarifies + conventional activated sludge	_64.1	Blair et al., 2015
		10 - 22 ng/l	Primary treatment + Orbal oxidation ditch + UV disinfection	40 - 100	Sun et al., 2014a
5	Trimethoprim	570 ng/l	Grit channels + primary clarifies + conventional activated sludge	_53.1	Blair et al., 2015
		5 mg/kg dry weight sludge	Anaerobic sludge digestion	98	Narumiya et al., 2013
6	Erythromycin	15 mg/kg dry weight sludge	Anaerobic sludge digestion	~45	Narumiya et al., 2013

7	Ofloxacin	2100 ng/l	Grit channels + primary clarifies + conventional activated sludge	_124.2	Blair et al., 2015
		10 mg/kg dry weight sludge	Anaerobic sludge digestion	~45	Narumiya et al., 2013
8	Ciprofloxacin	2200 ng/l	Grit channels + primary clarifies + conventional activated sludge	_88.6	Blair et al., 2015
	Lipid regulator				
9	Gemfibrozi	8500 ng/l	A^2/O	92	Yu et al., 2013
		190 ng/l	Grit channels + primary clarifies + conventional activated sludge	50.8	
10	Bezafibrate	50 mg/kg dry weight sludge	Anaerobic sludge digestion	~30	Narumiya et al., 2013
11	Clorfibric acid	420 ng/l	Oxidation ditch	81	Yu et al., 2013
	Nonsteroidal anti-inflammatory drugs				
12	Ibuprofen	5650 ng/l	Modified Bardenpho process	98	Yu et al., 2013
		4500 ng/l	Grit channels + primary clarifies + conventional activated sludge	99.7	Blair et al., 2015
		130 - 450 ng/l	Primary treatment + Orbal oxidation ditch + UV disinfection	60 - 90	Sun et al., 2014a
13	Diclofenac	580 ng/l	Bardenpho process	80	Yu et al., 2013
		20 - 70 mg/l	Primary treatment + Orbal oxidation ditch + UV disinfection	10 - 60	Sun et al., 2014a
		50 mg/kg dry weight sludge	Anaerobic sludge digestion	~20	Narumiya et al., 2013
14	Paracetamol	218000 ng/l	Modified Bardenpho process	99	Yu et al., 2013
15	Naproxen	870 ng/l	Modified Bardenpho process	94	Yu et al., 2013
		3000 ng/l	Grit channels + primary clarifies + conventional activated sludge	96.2	Blair et al., 2015
16	Aspirin	930 ng/l	Modified Bardenpho process	92	Yu et al., 2013
17	Ketoprofen	70 - 220 ng/l	Primary treatment + conventional activated sludge + tertiary treatment (ultrafiltration and ozonation)	_30 - 80	Sun et al., 2014a
	Beta-blocker				
18	Atenolol	255 ng/l	Grit tanks + primary sedimentation + bioreactor + clarifiers	47.1	Roberts et al., 2016
19	Metoprolol	379 ng/l		52.9	Roberts et al., 2016
20	Sotalol	711 ng/l		_6.8	Roberts et al., 2016
21	Propanolol	151 ng/l	Grit tanks + primary sedimentation + bioreactor + clarifiers	49.9	Roberts et al., 2016
		8 mg/kg dry weight sludge	Anaerobic sludge digestion	60	Narumiya et al., 2013
	Antidepressant				
22	Fluxetine	51.1 ng/l	Grit tanks + primary sedimentation + bioreactor + clarifiers	68.2	Roberts et al., 2016
		50 ng/l	Grit channels + primary clarifies + conventional activated sludge	23.1	Blair et al., 2015
23	Diazepam	8 mg/kg dry weight sludge	Anaerobic sludge digestion	~90	Narumiya et al., 2013
	Anticonvulsants				
24	Carbamazepine	589 ng/l	Grit tanks + primary sedimentation + bioreactor + clarifiers	_16.3	Roberts et al., 2016
		350 mg/l	Oxidation ditch	81	Yu et al., 2013
		10 mg/l	Grit channels + primary clarifies + conventional activated sludge	_92.4	Blair et al., 2015
	Preservatives				

25	Methylparaben	567 ng/l	Primary treatment + conventional activated sludge + tertiary treatment (ultrafiltration and ozonation)	98.8	Li et al., 2015a
		150 - 270 ng/l	Primary treatment + Orbal oxidation ditch + UV disinfection	81.6 - 91	Sun et al., 2014a
26	Ethylparaben	140 ng/l	Primary treatment + conventional activated sludge + tertiary treatment (ultrafiltration and ozonation)	99.8	Li et al., 2015a
27	Propylparaben	438 ng/l	Primary treatment + conventional activated sludge + tertiary treatment (ultrafiltration and ozonation)	99.9	Li et al., 2015a
		130 - 400 ng/l	Primary treatment + Orbal oxidation ditch + UV disinfection	80 - 100	Sun et al., 2014a
28	Butylparaben	27.9 ng/l	Primary treatment + conventional activated sludge + tertiary treatment (ultrafiltration and ozonation)	99.7	Li et al., 2015a
	Disinfectants				
29	Triclosan	1854 ng/L	Grit tanks + primary sedimentation + bioreactor + clarifiers	99.8	Roberts et al., 2016
		4400 ng/l	Modified Bardenpho process	>95	Yu et al., 2013
		300 ng/l	Grit channels + primary clarifies + conventional activated sludge	55.3	Blair et al., 2015
		8 mg/kg dry weight sludge	Anaerobic sludge digestion	~25	Narumiya et al., 2013

As depicted from Table [2], it can be seen that the removal efficiency of PPCPs by Waste Water Treatment Plant (WWTPs) is not 100% efficient for all compounds. This shows weakness in the used technology which in simple terms can cause contamination to the environment in the aftermath of the treatment process (i.e, after discharge to the surface water). Generally, waste water-treatment plants (WWTPs) do not fully remove pharmaceuticals due to lack of proper design.[6, 7, 8, 9] Other studies have shown that the major and common method of infectious medical waste treatment method in the developed countries is by incineration in which waste is burned to high temperatures (i.e., 1200^{o}C) and in the process the volume size is reduced and what remains is residual ash. The remaining ash is then dumped at landfill sites and then buried. This process ensures that infectious waste is sterilized and reduced in volume size to ash which in turn reduces cost of transportation to landfill sites.[66,67] However, the main disadvantage of incineration of medical waste is the emissions and toxic pollutants dioxins, furans, and mercury arising from burning of waste. Due to different compositions burning of infectious waste produces toxic gases into the environment hence this method is highly controlled in developed countries as the emitted harmful gases released into the satmosphere may affect human health.[66, 68] In order to eliminate the disposal of ash to the landfill facility to be buried which might cause further risk as it might enter into the ground water environment, the pharmaceutical ash can be made into sludge. This pharmaceutical sludge could be used for the production and construction materials called bricks. The use of this method is highly profitable and essentially reduces exploitation of natural raw materials.[43]

3. CONCLUSION

The advantages of pharmaceuticals to treat humans and animals must outweigh its disadvantages of polluting the environment in order to be considered valid for its cause. However, looking at the rate at which pollution from pharmaceutical waste is spreading across the globe there is a lot to be desired. In as much as all players involved are doing their best to mitigate the situation little has been done in focusing about the future trend of pollution arising from pharmaceutical waste. This is partly due to lack of established policies, legislation, sources, handling, methods, testing standards and not forgetting the risks that await us now and in the near future. In conclusion, if the sub divisions of pharmaceutical waste management can efficiently work back to back, environmental pollution and dangers to human health can reduce significantly today and in the years to come. Failure to efficiently work in one policy or one portion of pharmaceutical waste management leads to the declaration of the entire pharmaceutical waste management process redundant.

ACKNOWLEDGEMENTS

The author wishes to acknowledge Mr Musa Jacob Khatri, Lecturer, School of Engineering, University of Zambia (UNZA), for his support and encouragement throughout this work.

REFERENCES

1. Pruss, A., Giroult, E., Rushbrook, P. (eds)., "Safe management of wastes from healthcare activities" World Health Organization. Geneva. 1999; 3-4.
2. Evangelos Voudrias, Lambrini Goudakou, Marianthi Kermenidou and Aikaterini Softa, "Composition and production rate of pharmaceutical and chemical waste from Xanthi General Hospital in Greece", Waste Management, 2012; 32 springer, 1442–1452.
3. Vallini, G., Townend, W.K., Pharmaceutical waste: as in the Titanic we are only seeing the tip of the iceberg-editorial. Waste Management and Research 2010; 28(9): 767–768.
4. Chongqing Wang et al., "Separation of aluminum and plastic by metallurgy method for recycling waste pharmaceutical blisters", Journal of Cleaner Production, Elsevier, 2015; 102: 378 – 383.
5. Malkan, S. Global trends in responsible healthcare waste management – A perspective from Health Care without Harm. Waste Manag, 2005; 25: 567-572.
6. Carlos Rodrı´guez-Navas, Erland Bjo¨rklund, Søren A Bak, Martin Hansen, Kristine A. Krogh, Fernando Maya, Rafael Forteza and Vı´ctor Cerda, "Pollution Pathways of Pharmaceutical Residues in the Aquatic Environment on the Island of Mallorca, Spain", Arch Environ Contam Toxicol, 2013; 65: 56–66.
7. Zhou JL, Zhang ZL, Banks E, Grover D, Jiang JQ, Pharmaceutical residues in wastewater treatment works effluents and their impact on receiving river water. J Hazard Mater, 2009; 166: 655–661.
8. Murray KE, Thomas SM, Bodour AA, Prioritizing research for trace pollutants and emerging contaminants in the freshwater environment. Environ Pollut, 2010; 158: 3462–3471.
9. Jelic´ A, Petrovic´ M, Barcelo´ D, Pharmaceuticals in drinking water. Springer, Berlin, 2012; 1–24.
10. Thiele-Bruhn S., Pharmaceutical antibiotic compounds in soils—a review. J Plant Nutr Soil Sci., 2003; 166: 145–167.
11. Oppel J, Broll G, Lo¨ffler D, Meller M, Ro¨mbke J, Ternes T, Leaching behaviour of pharmaceuticals in soil-testing-systems: a part of an environmental risk assessment for groundwater protection. Sci Total Environ, 2004; 328: 265–273.
12. Hansen M, Krogh KA, Halling-Sorensen B, Bjorklund E, Determination of ten steroid hormones in animal waste manure and agricultural soil using inverse and integrated clean-up pressurized liquid extraction and gas chromatography-tandem mass spectrometry. Anal Methods, 2011; 3: 1087–1095.
13. Emma J. Rosi-Marshall and Todd V. Royer, Pharmaceutical Compounds and Ecosystem Function: An Emerging Research Challenge for Aquatic Ecologists, Ecosystems, 2012; 15: 867–880.
14. Pailler JY, Guignard C, Meyer B, Iffly JF, Pfister L, Hoffmann L, Krein A., Behaviour and fluxes of dissolved antibiotics, analgesics and hormones during flood events in a small heterogeneous catchment in the Grand Duchy of Luxembourg. Water Air Soil Pollut, 2009; 203: 79–98.
15. Weyrauch P, Matzinger A, Pawlowsky-Reusing E, Plume S, von Seggern D, Heinzmann B, Schroeder K, Rouault P., Contribution of combined sewer overflows to trace contaminant loads in urban streams. Water Res., 2010; 44: 4451–62.
16. Phillips PJ, Smith SG, Kolpin DW, Zaugg SD, Buxton HT, Furlong ET, Esposito K, Stinson B., Pharmaceutical formulation facilities as sources of opioids and other pharmaceuticals to wastewater treatment plant effluents. Environ Sci Technol, 2010; 44(13): 4910–16.
17. Larsson, D. G. J., de Pedro, C., & Paxeus, N., Effluent from drug manufactures contains extremely high levels of pharmaceuticals. J. Hazardous Materials, 2007; 148: 751–755.
18. Fick J, Soderstrom H, Lindberg RH, Phan C, Tysklind M, Larsson DGJ., Contamination of surface, ground and drinking water from pharmaceutical production. Environ Toxicol Chem, 2009; 28(12): 2522–7.
19. Tamara L. Sorell, Approaches to the Development of Human Health Toxicity Values for Active Pharmaceutical Ingredients in the Environment, The AAPS Journal (2015); DOI: 10.1208/s12248-015-9818-5.
20. Jimoh O. Tijani & Ojo O. Fatoba & Leslie. F. Petrik, A Review of Pharmaceuticals and Endocrine-Disrupting Compounds: Sources, Effects, Removal, and Detections, Water Air Soil Pollut, 2013; 224: 1770.
21. Environmental Protection Authority Victoria (EPA 2016), Point and nonpoint sources of water pollution Retrieved October 12-2016, from: http://www.epa.vic.gov.au.
22. European Environmental Agency, 2008, Diffuse sources, Retrieved October 12-2016, from:http://www.eea.europa.eu/themes/water/waterpollution/diffuse-sources.
23. Manfred Sengl and Sonja Krezmer, Proficiency tests for pharmaceuticals in different waters, Accred Qual Assur, 2003; 8: 523–529.
24. Daughton CG, Ternes TA (1999) Environmental Health Perspectives, 107: 907–938.
25. Despo Fatta-Kassinos & Sureyya Meric & Anastasia Nikolaou, Pharmaceutical residues in environmental waters and wastewater: current state of knowledge and future research, Anal Bioanal Chem. 2010; 399: 251–275.
26. Luisa Patrolecco & Silvio Capri & Nicoletta Ademollo, Occurrence of selected pharmaceuticals in the principal sewage treatment plants in Rome (Italy) and in the receiving surface waters, Environ

Sci Pollut Res, Springer-Verlag Berlin Heidelberg, (2014); DOI 10.1007/s11356-014-3765-z.
27. Randhir P. Deo, Pharmaceuticals in the Surface Water of the USA: A Review, Curr Envir Health Rpt, 2014; 1: 113–122.
28. Foluso O. Agunbiade & Brenda Moodley, Environ Monit Assess, 2014; 186: 7273–7291.
29. K.O. K'oreje, L. Vergeynst D. Ombaka, P. De Wispelaere, M. Okoth, H. Van Langenhove, K. Demeestere, Occurrence patterns of pharmaceutical residues inwastewater, surface water and groundwater of Nairobi and Kisumu city, Kenya, Chemosphere, 2016; 149: 238 – 244.
30. Mu-Chen Lu, Yao Yin Chen, Mei-Rung Chiou, Men Yu Chen, Huan-Jung Fan (2016), Occurrence and treatment efficiency of pharmaceuticals in landfill leachates, Waste Management, http://dx.doi.org/10.1016/j.wasman.2016.03.029. www.elsevier.com/locate/wasman.
31. Jianlong Wang and Shizong Wang, Removal of pharmaceuticals and personal care products (PPCPs) from wastewater: A review, Journal of Environmental Management, 2016; 182: 620 – 640.
32. Zakiya Hoyett , Marcia Allen Owens, Clayton J. Clark, Michael Abazinge, A comparative evaluation of environmental risk assessment strategies for pharmaceuticals and personal care products, Ocean & Coastal Management, 2016; 127: 74 – 80.
33. Leslie Cizmas, Virender K. Sharma, Cole M. Gray, Thomas J. McDonald, Pharmaceuticals and personal care products in waters:occurrence, toxicity and risk, Environ Chem Lett, (2015); DOI 10.1007/s10311-015-0524-4.
34. Martins, A.F., Vasconcelos, T.G., Henriques, D.M., Frank, C.d.S., K€onig, A., Kümmerer, K., Concentration of ciprofloxacin in Brazilian hospital effluent and preliminary risk assessment: a case study. Clean Soil Air Water, 2008; 36(3): 264-269. http://dx.doi.org/10.1002/clen.200700171.
35. Ali Sharif & Muhammad Ashraf & Aftab Ahmed Anjum & Aqeel Javeed & Imran Altaf & Muhammad Furqan Akhtar & Mateen Abbas & Bushra Akhtar & Ammara Saleem, Pharmaceutical wastewater being composite mixture of environmental pollutants may be associated with mutagenicity and genotoxicity, Environ Sci Pollut Res, (2015): DOI 10.1007/s11356-015-5478-3.
36. Velagaleti R, Burns P., The Industrial ecology of pharmaceutical raw materials and finished products with emphasis on supply chain management activities the industrial ecology of pharmaceutical raw materials and finished products with emphasis on supply chain management activities (2006).
37. Anyakora C, Nwaeze K, Awodele O, Nwadike C, Arbabi M, Coker H, Concentrations of heavy metals in some pharmaceutical effluents in Lagos, Nigeria, J Environ Chem Ecotoxicol, 2011; 3: 25–31.
38. Bruce GM, Pleus RC, Snyder SA, Toxicological relevance of pharmaceuticals in drinking water. Environ Sci Technol, 2010; 44: 5619–5626. doi:10.1021/es1004895.
39. Schaider LA, Rudel RA, Ackerman JM, Dunagan SC, Brody JG, Pharmaceuticals, perfluorosurfactants and other organic wastewater compounds in public drinking water wells in a shallow sand and gravel aquifer. Sci Total Environ, 2014; 468–469: 384–393. doi:10.1016/j.scitotenv.2013.08.067.
40. WHO (2011) Pharmaceuticals in drinking-water. Report No.: WHO/ HSE/WSH/11.05. Geneva, Switzerland:WorldHealthOrganization.http://www. who.int/water_sanitation_health/publications/2011/pharmaceuticals_20110601.pdf.
41. Bergman A, Heindel JJ, Kasten T, Kidd KA, Jobling S, Neira M, Zoeller RT, Becher G, Bjerregaard P, Bornman R, Brandt I, Kortenkamp A, Muir D, Drisse MB, Ochieng R, Skakkebaek NE, Byle´hn AS, Iguchi T, Toppari J, Woodruff TJ, The impact of endocrine disruption a consensus statement on the state of the science. Environ Health Perspect, 2013; 121(4): A104–A106.
42. Dimitrios P. Komilis, Issues on medical waste management research, Waste Management, 2016; 48: 1–2.
43. M. Yamuna Rani & D. Bhagawan & V. Himabindu & V. Venkateswara Reddy & P. Saritha "Preparation and characterization of green bricks using pharmaceutical industrial wastes", Environ Sci Pollut Res: (2015); DOI 10.1007/s11356-015-5191-2.
44. Thomas G. Bean, Ed Bergstrom, Jane Thomas-Oates, Amy Wolff, Peter Bartl, Bob Eaton, Alistair B. A. Boxall, Evaluation of a Novel Approach for Reducing Emissions of Pharmaceuticals to the Environment, Environmental Management: (2016); DOI 10.1007/s00267-016-0728-9.
45. Daughton CG, Ruhoy IS, Environmental footprint of pharmaceuticals: the significance of factors beyond direct excretion to sewers. Environ Toxicol Chem, 2009; 28(12): 2495–2521. doi:10.1897/ 08-382.1.
46. Li, J.-D., Cai, Y.-Q., Shi, Y. L., Mou, S. F., & Jiang, G. B., Determination of sulfonamide compounds in sewage and river by mixed hemimicelles solid-phase extraction prior to liquid chromatography–spectrophotometry. Journal of Chromatography, 2007; A, 1139: 178–184.
47. Persson M, Sabelstrom E, Gunnarsson B, Handling of unused prescription drugs—knowledge, behaviour and attitude among Swedish people. Environ Int, 2009; 35(5): 771–774. doi:10.1016/j. envint.2008.10.002.
48. H. Matsuo, H. Sakamoto, K. Arizono, R. Shinohar, Behavior of Pharmaceuticals in Waste Water Treatment Plant in Japan, Bull Environ Contam Toxicol, 2011; 87: 31–35.
49. Carolina Nebot & Raquel Falcon & Kenneth G. Boyd & Stuart W. Gibb, Introduction of human pharmaceuticals from wastewater treatment plants into the aquatic environment: a rural perspective,

Environ Sci Pollut Res, (2015): DOI 10.1007/s11356-015-4234-z.
50. M.I. Tabash, R.A. Hussein, A.H. Mahmoud, M.D. El-Borgy, B.A. Abu-Hamad, Impact of an intervention programme on knowledge, attitude and practice of healthcare staff regarding pharmaceutical waste management, Gaza, Palestine, Public Health, 2016; xxx: i – ii.
51. Anna Birna Almarsdo´ t t i r and Janine M. Traulsen, Rational use of medicines – an important issue in pharmaceutical policy, Pharm World Sci, 2005; 27: 76–80.
52. Benjamin D. Blair, Potential Upstream Strategies for the Mitigation of Pharmaceuticals in the Aquatic Environment: a Brief Review, Curr Envir Health Rpt, 2015; 3: 153–160.
53. Nora A. Doerr-MacEwen and Murray E. Haight, Expert Stakeholders' Views on the Management of Human Pharmaceuticals in the Environment, Environ Manage, 2006; 38: 853–866.
54. Bell KY, Wells MJM, Traexler KA, Pellegrin M, Morse A, Bandy J, Emerging pollutants. Water Environ Res, 2011; 83: 1906–1984.
55. Breivik K, Gioia R, Chakraborty P, Zhang G, Jones KC, Are reductions in industrial organic contaminants emissions in rich countries achieved partly by export of toxic wastes? Environ Sci Technol, 2011; 45(21): 9154–9160. doi:10.1021/es202320c.
56. Esplugas S, Bila DM, Krause LGT, Dezotti M, Ozonation and advanced oxidation technologies to remove endocrine disrupting chemicals (EDCs) and pharmaceuticals and personal care products (PPCPs) in water effluents J Hazard Mater, 2007; 149(3): 631–642. doi:10.1016/j.jhazmat.2007.07.073.
57. Manickum T, John W., Occurrence, fate and environmental risk assessment of endocrine disrupting compounds at the wastewater treatment works in Pietermaritzburg (South Africa). Sci Total Environ, 2014; 468–469: 584–597. doi:10.1016/j.scitotenv.2013.08.041.
58. Focazio MJ, Kolpin DW, Barnes KK, Furlong ET, Meyer MT, Zaugg SD, Barber LB, Thurman ME, A national reconnaissance for pharmaceuticals and other organic wastewater contaminants in the United States—II) untreated drinking water sources. Sci Total Environ, 2008; 402: 201–216. doi:10.1016/j.scitotenv.2008.02.021.
59. Jin X, Peldszus S, Selection of representative emerging micropollutants for drinking water treatment studies: a systematic approach. Sci Total Environ, 2012; 414: 653–663. doi:10.1016/j. scitotenv.2011.11.035.
60. Padhye LP, Yao H, Kung'u FT, Huang CH, Year-long evaluation on the occurrence and fate of pharmaceuticals, personal care products and endocrine disrupting chemicals in an urban drinking water treatment plant. Water Res., 2014; 51: 266–276 doi:10.1016/j.watres.2013.10.070.
61. Swati M, Rema T, Joseph K., Hazardous organic compounds in urban municipal solid waste from a developing country. J Hazard Mater, 2008; 160: 213–219. doi:10.1016/j.jhazmat.2008.02.111.
62. M. Deegan, B. Shaik, K. Nolan, K. Urell, M. Oelgemöller, J. Tobin, A. Morrissey, Treatment options for wastewater effluents from pharmaceutical companies, Int. J. Environ. Sci. Tech. 2011; 8(3): 649-666.
63. Elliott Steen Windfeld and Marianne Su-Ling Brooks, Medical waste management - A review, Journal of Environmental Management, 2015; 163: 98 – 108.
64. Lee, B.-K., Ellenbecker, M.J., Moure-Ersaso, R., Alternatives for treatment and disposal cost reduction of regulated medical waste. Waste Manag. 2004; 24: 143-151. http://dx.doi.org/10.1016/j.wasman.2003.10.008.
65. Klangsin, P., Harding, A., Medical waste treatment and disposal methods used by hospitals in Oregon, Washington and Idaho. J. Air Waste Manag. Assoc. 1998; 48: 516-526. http://dx.doi.org/10.1080/10473289.1998.10463706.
66. Elliott Steen Windfeld and Marianne Su-Ling Brooks, Medical waste management - A review, Journal of Environmental Management, 2015; 163: 98–108.
67. Lee, C.C., Huffman, G.L., Review: medical waste management/incineration. J. Hazard. Mater. 1996; 48: 1-30. http://dx.doi.org/10.1016/0304-3894(95)00153-0.
68. Insa, E., Zamorano, M., Lopez, R., Critical review of medical waste legislation in Spain. Resour. Conserv. Recycl. 2010; 54: 1048-1059. http://dx.doi.org/10.1016/ j.resconrec.2010.06.005.
69. Foluso O. Agunbiade & Brenda Moodley, Environ Monit Assess, 2014; 186: 7273–7291.
70. Haggard, B. E., Galloway, J. M., Green, W. R., & Meyer, M. T., Pharmaceuticals and other organic chemicals in selected north-central and northwestern Arkansas streams. Journal of Environmental Quality, 2006; 35(4): 1078–1087.
71. Benotti, M. J., Trenholm, R. A., Vanderford, B. J., Holady, J. C., Stanford, B. D., & Snyder, S. A. Pharmaceuticals and endocrine disrupting compounds in U.S. drinking water. Environmental Science and Technology, 2009; 43: 597–603.
72. Watkinson, A. J., Murby, E. J., Kolpin, D. W., & Costanzo, S. D., The occurrence of antibiotics in an urban watershed: from wastewater to drinking water. Science of the Total Environment, 2009; 407: 2711–2723.
73. Benito-Pena, E., Partal-Rodera, A. I., Leon-Gonzalez, M. E., & Moreno-Bondi, M. C. Evaluation of mixed mode solid phase extraction cartridges for the preconcentration of Environ Monit Assess, 2014; 186: 7273–7291 7289. beta-lactam antibiotics in wastewater using liquid chromatography with UV-DAD detection. Analytica Chimica Acta, 556: 415–422.

74. Hirsch, R., Ternes, T. A., Haberer, K., & Kratz, K. L., Occurrence of antibiotics in the aquatic environment. Science of the Total Environment, 1999; 225: 109–118.
75. Li, D., Yu, T., Zhang, Y., Yang, M., Li, Z., Liu, M., & Qi, R., Antibiotic resistance characteristics of environmental bacteria from an oxytetracycline productionwastewater treatment plant and the receiving river. Applied and Environmental Microbiology, 2010; 76(11): 3444–3451.
76. Lindqvist, N., Tuhkanen, T., & Kronberg, L., Occurrence of acidic pharmaceuticals in raw and treated sewages and in receiving waters. Water Research, 2005; 39: 2219–2228.
77. Rabiet, M., Togola, A., Brissaud, F., Seidel, J. L., Budzinski, H., & Elbaz-Poulichet, F., Consequences of treated water recycling as regards pharmaceuticals and drugs in surface and ground waters of a medium-sized Mediterranean Catchment. Environmental Science and Technology, 2006; 40(17): 5282–5288.
78. Loraine, G. A., & Pettigrove, M. E., Seasonal variations in concentrations of pharmaceuticals and personal care products in drinking water and reclaimed wastewater in Southern California. Environmental Science and Technology, 2006; 40(3): 687–695.
79. Rodil, R., Quintana, J. B., López-Mahía, P., Muniategui-Lorenzo, S., & Prada-Rodríguez, D., Multi-residue analytical method for the determination of emerging pollutants in water by solid-phase extraction and liquid chromatography–tandem mass spectrometry. Journal of Chromatography, 2009; A, 1216: 2958–2969.
80. W.C. Li., Occurrence, sources and fate of pharmaceuticals in aquatic environment and soil, Environmental Pollution, 2014; 187: 193 – 201.
81. Thach AV, Brown CM, Pope N., Consumer perceptions about a community pharmacy-based medication take back program. J Environ Manag, 2013; 127: 23–27. doi:10.1016/j.jenvman.2013.04.025.