

Pharmaceuticals in Surface Water and Waste Water Treatment Plant Effluent Around the World – A Review

Pharmaceuticals and personal care products are “Emerging Contaminants” which are widely exist around word at trace amount. Evidence by researchers showed PPCPs had potential risk on humans and the environment.

This paper reviews the occurrence of several pharmaceuticals and personal care products based on their studied frequencies in the literatures like naproxen, ibuprofen or Carbamazepine. Previous studies also showed that more advanced area have a higher concentration of the PPCPs, like north America and Europe. Currently, many useful techniques like GC/MS, LC-MS/MS, HPLC/UV and UPLC/MS/MS can precisely analyze the PPCPs from the surface water and effluent of the wastewater.

The paper also reviews the treatments of remove those PPCPs. To remove PPCPs in wastewater and surface water, conventional physiochemical methods were not suitable. Advanced methods like reverse osmosis, nano-filtration and constructed wetlands can effectively remove PPCPs. Advanced techniques such as reverse osmosis, nano-filtration and constructed wetlands showed great removal efficiency in studies and in the application of many regions.

Keywords: Pharmaceutical personal care products, analytical methods, trace, removal

1. INTRODUCTION (ARIAL, BOLD, 11 FONT, LEFT ALIGNED, CAPS)

Pharmaceuticals and personal care products (PPCPs) are one group of “Emerging Contaminants,” a name that has been used by the EPA since the 1990s [1]. PPCPs include a diverse collection of thousands of chemical substances, including prescription and over the counter therapeutic drugs, veterinary drugs, fragrances, cosmetics, sun-screen products, diagnostic agents, and nutraceuticals [2].

PPCPs have been present in ecosystems for decades at a trace level concentration i.e., at the µg/l or even ng/l) [3]. They were not studied at first because of the technology limitation for detection. Now with advances in technology that provide the ability to detect and quantify these “undetectable” chemicals, they can be identified and their effects on humans and the environment can be studied.

PPCPs have been a serious problem as they are widely used and some of them are harmful to the environment and humans. From 1999 to 2000, Barnes *et.al.* [4] conducted a nationwide survey in the US, and identified the occurrence 95 different pharmaceuticals, hormones, and other organic wastewater contaminants (OWCs) in 139 streams in 30 states. The survey showed that at least one OWC was detected in 80% of the streams sampled, with 82 of the 95 analyzed OWCs determined in this study detected in at least one sample. Also, PPCPs can easily enter the environment, for instance through manufacturing plants, effluents of sewage treatment plants, household waste, and landfill effluent [5]. In 2009, Cheri Garvin, CEO of the Leesburg Pharmacy, made a statement about secure and responsible drug disposal, that U.S. manufacturers had legally released 271 million pounds of drugs into the environment, and an estimated 250 million pounds of pharmaceuticals and contaminated packaging were discarded by hospitals and long-term care facilities [6].

2. METHODS USED FOR PPCPS ANALYSIS

2.1 Extraction/concentration

PPCPs appear in the environment at trace concentrations. In response to the low concentrations, most analytical methods were designed to ng/l detection limit. Most analytical instruments cannot

directly detect the chemicals in concentration of ng/l, so an extraction step is applied first. Table 1 shows some extraction techniques in which the solid-phase extraction (SPE) is the most common one that was used in the extraction of contaminants.

Table 1: Extraction techniques with references

Extraction techniques	Liquid-liquid	Soxhlet	Steam distillation	Solid-phase extraction
References	Yook <i>et al.</i> 1994 Holm <i>et al.</i> 1995	Bennie <i>et al.</i> 1997 Pryor <i>et al.</i> 2002	Kubeck and Naylor 1990 Fowler <i>et al.</i> 1998	Camel 2003

The basic approach [7] for solid-phase extraction involves passing the liquid sample through a column, a cartridge, a tube or a disk containing an adsorbent that retains the analytes. After all samples have been passed through the sorbent, retained analytes are subsequently recovered upon elution with an appropriate solvent.

2.1.2 Gas Chromatography

Gas Chromatography (GC) [8] works by injecting a liquid sample into a heated injection chamber, where the compounds are quickly vaporized and swept by a carrier gas (usually helium) onto a silica chromatography capillary column internally coated with a stationary phase. The column is in an oven where the temperature can be changed. The individual compounds will separate as they flow through the column based on their boiling point, affinity for the stationary phase, and temperature profile of the GC oven. A detector then monitors the compounds as they leave the column. Mass spectrometry (MS) is one of the most useful and common detectors due to its sensitivity and superior selectivity. MS detects [3] analytes based on mass to charge ratio (m/z), as analytes must first be ionized. After ionization, they can be identified based on their fragmentation patterns.

2.1.3 Liquid Chromatography

Liquid Chromatography (LC) is also a widely used analytical technique which consists of a solvent pump, sample injector, analytical column, and a detector. Unlike the GC, the separation of analytes in LC occurs in the liquid phase. Usually LC [3] is coupled with mass spectrometry to be more sensitive and selective.

Modern LC-Mass Spectrometers (MS) methods use high pressure liquid chromatography (HPLC) instrumentation. In HPLC, the sample is forced by a liquid at high pressure (the mobile phase) through a column that is packed with a stationary phase composed of irregularly or spherically shaped particles chosen or derivatized to accomplish particular types of separations.

3. CURRENT OCCURRENCE OF PPCPS AROUND THE WORLD

Nine common PPCPs were selected based on their frequencies showed in the literatures. Table 2 gives the general information of these PPCPs' type, extraction methods, and analytical techniques used for the individual studies. Data were compiled from references [9], [10], [11], [12], [13], [14], [15], [16], [17], [18], [19], [20], [21], [22], [23], [24], [25], [26], [27], [28], [29].

Table 2: Methods for selected PPCPs

Target Compound	Type	Extraction	Chromatography	Citation
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Carbamazepine	Anticonvulsant	SPE	Derivatize GC/MS HPLC/UV LC/MS LC-MS/MS	Benner et al. 2008. Benotti et al. 2008. Gomez et al. 2008. Kim et al. 2007. Loos et al. 2009, 2013. Melo et al. 2013. Miège et al. 2008. Pal et al. 2010. Petrović et al. 2003. Radjenović et al. 2009.
Trimethoprim	Pyrimidine antibiotic	SPE	Derivatize GC/MS UPLC/MS/MS HPLC/UV LC-MS/MS	Benner et al. 2008. Boleda et al. 2011. Benotti et al. 2008. Gomez et al. 2008. Kim et al. 2007. Loos et al. 2013. Miège et al. 2008. Pal et al. 2010. Radjenović et al. 2009.
Diclofenac	Analgesic	SPE	Derivatize GC/MS UPLC/MS/MS HPLC/UV LC-MS/MS LC-MS	Benner et al. 2008. Boleda et al. 2011. Benotti et al. 2008. Gomez et al. 2008. Kim et al. 2007. Loos et al. 2009., 2013. Melo et al. 2013. Miège et al. 2008. Pal et al. 2010. Petrović et al. 2003. Radjenović et al. 2009.
Iopromide	X-ray Contrast Media	SPE	UPLC/MS/MS HPLC/UV LC-MS/MS	Benner et al. 2008. Boleda et al. 2011. Kim et al. 2007. Loos et al. 2013. Miège et al. 2008.
Ibuprofen	Analgesics	SPE	Derivatize GC/MS UPLC/MS/MS HPLC/UV LC-MS/MS LC-MS	Benner et al. 2008. Boleda et al. 2011. Gomez et al. 2008. Kim et al. 2007. Loos et al. 2009, 2013. Melo et al. 2013. Miège et al. 2008. Pal et al. 2010. Pérez et al. 2000. Petrović et al. 2003. Radjenović et al. 2009.
Naproxen	non-steroidal anti-inflammatory drug	SPE	GC/MS UPLC/MS/MS HPLC/UV LC-MS/MS LC-MS GC/ECD	Benner et al. 2008. Boleda et al. 2011. Benotti et al. 2008. Gomez et al. 2008. Kim et al. 2007. Loos et al. 2009, 2013. Miège et al. 2008. Pal et al. 2010. Pérez et al. 2000. Petrović et al. 2003. Radjenović et al. 2009.
Sulfamethoxazole	Sulfonamide antibiotic	SPE	Derivatize GC/MS UPLC/MS/MS HPLC/UV LC-MS/MS	Benner et al. 2008. Boleda et al. 2011. Benotti et al. 2008. Gomez et al. 2008. Kim et al. 2007. Loos et al. 2013. Miège et al. 2008. Pal et al. 2010. Radjenović et al. 2009.

Gemfibrozil	Antilipemic	SPE	Derivatize GC/MS UPLC/MS/MS LC-MS/MS LC-MS GC/ECD	Boleda et al. 2011. Benotti et al. 2008. Gomez et al. 2008. Kim et al. 2007. Loos et al. 2013. Melo et al. 2013. Miège et al. 2008. Pal et al. 2010. Pérez et al. 2000. Petrović et al. 2003. Radjenović et al. 2009.
Ketoprofen	Analgesic	SPE	Derivatize GC/MS LC-MS/MS LC-MS	Gomez et al. 2008. Melo et al. 2013. Miège et al. 2008. Pal et al. 2010. Petrović et al. 2003. Radjenović et al. 2009.

The following figures show the occurrence and the concentration ranges of these selected PPCPs in the surface water and in the effluent of the wastewater during 2006 to 2013 from literatures. From the selected PPCPs, data shows that PPCPs are widely existing around the world at trace concentrations. But some of the PPCPs appear at a very high concentration levels in certain region.

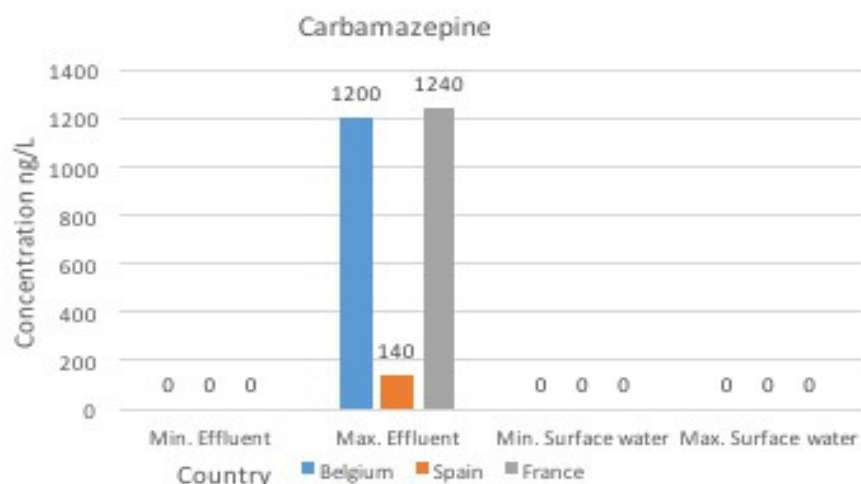
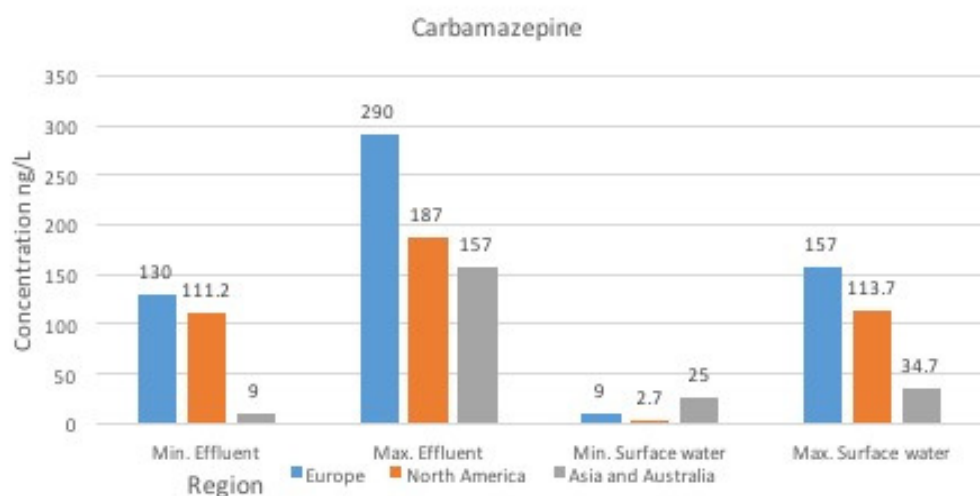


Figure 1: Occurrence and concentration of carbamazepine in effluent and surface water around world 2006-2013

Fig. 2 shows the range of carbamazepine concentration founded in the research in different area. Carbamazepine concentration in effluent was reported between 111.2 ng/L to 187 ng/L in North America, 130 ng/L to 290 ng/L in Europe, and 9 ng/L to 157 ng/L in Asia and Australia. The highest concentration was reported to 1200 ng/L in the effluent in Belgium, while in the other region, it was much lower in either effluent or surface water. It was 2.7 ng/L to 113.7 ng/L in North America, 9 ng/L to 157 ng/L in Europe, and 25 ng/L to 34.7 ng/L in Asia and Australia in surface water. In Spain and France, it was not reported in the surface water.

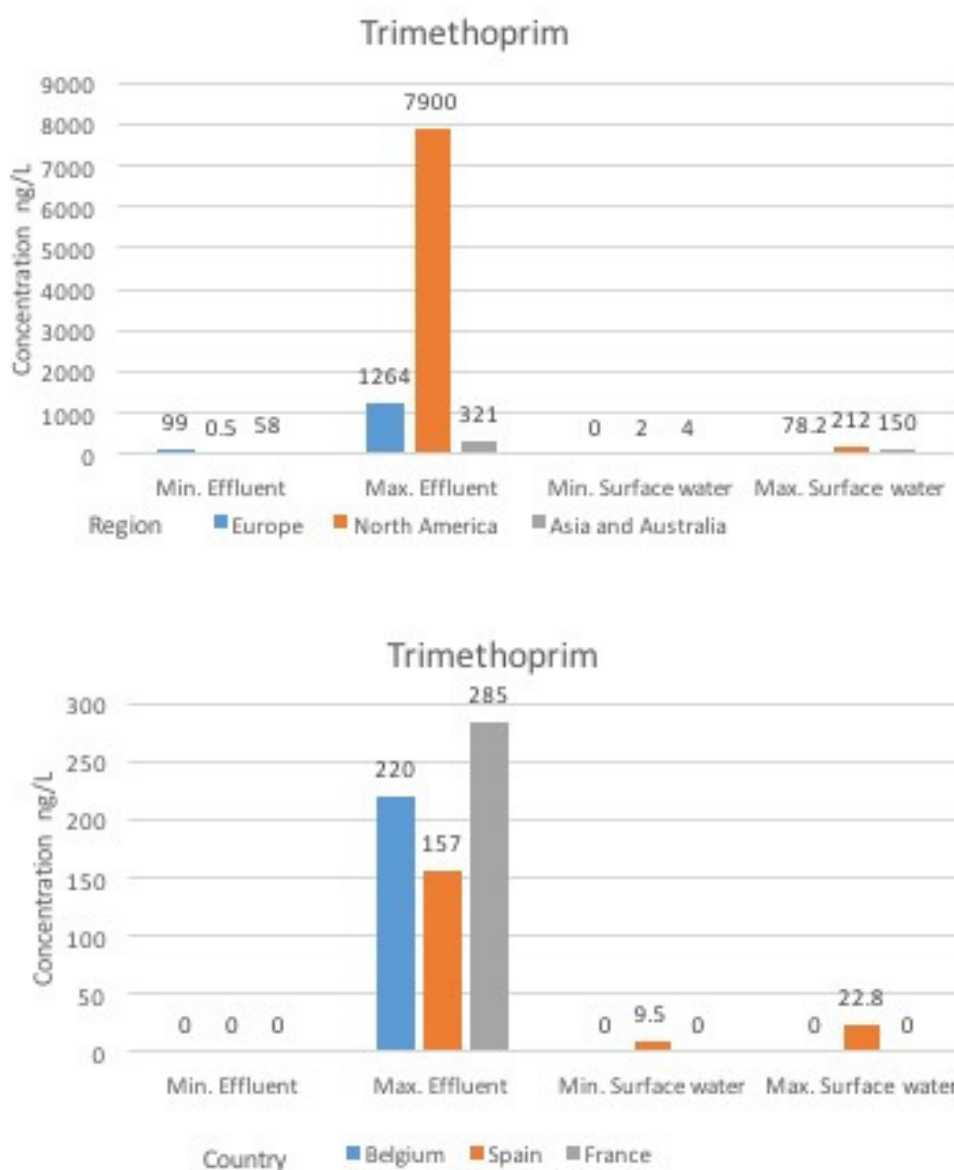


Figure 2: Occurrence and concentration of trimethoprim in effluent and surface water around world 2006-2013

The range of trimethoprim concentration founded in the research in different area areas of the world is shown in Fig 2. Concentration zero means not reported.

Trimethoprim concentration in effluent was reported between 0.5 ng/L to 7900 ng/L in North America, 99 ng/L to 1264 ng/L in Europe, and 58 ng/L to 321 ng/L in Asia and Australia. Trimethoprim concentrations were lower in surface than the concentration in effluent which was between 2 ng/L to 121 ng/L in North America, zero ng/L to 78.2 ng/L in Europe, and 4 ng/L to 150 ng/L in Asia and Australia. It was not reported in the surface water in Belgium and France.

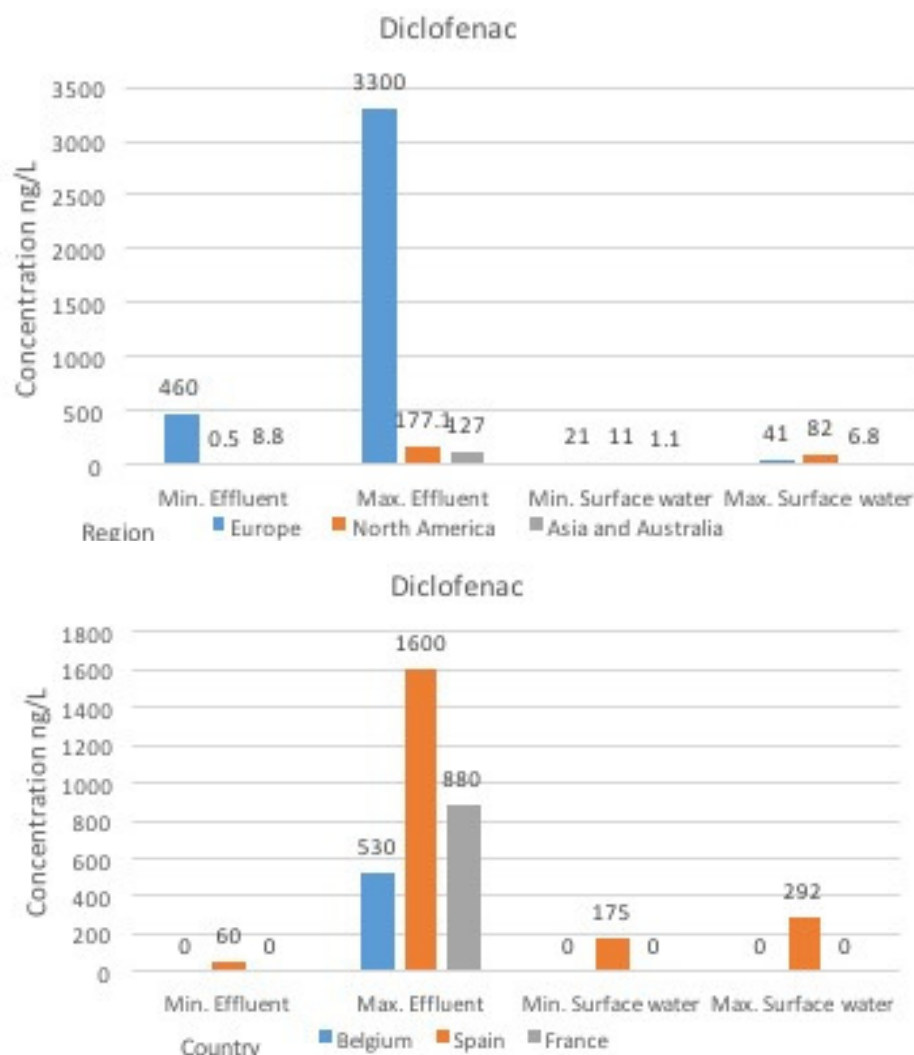


Figure 3 Occurrence and concentration of diclofenac in effluent and surface water around world 2006-2013

The Fig. 3 the range of diclofenac concentration founded in the research in different area is shown. Concentration zero means not reported.

Diclofenac concentrations were very low and were not reported in surface water in countries like Belgium and France.

Diclofenac concentration in effluent was reported between 0.5 ng/L to 177.1 ng/L in North America, 460 ng/L to 3300 ng/L in Europe, and 8.8 ng/L to 127 ng/L in Asia and Australia. It was 11 ng/L to 82 ng/L in North America, 21 ng/L to 41 ng/L in Europe, and 1.1 ng/L to 6.8 ng/L in Asia and Australia in surface water. In Spain, the highest concentration detected was 810 ng/L in surface water.

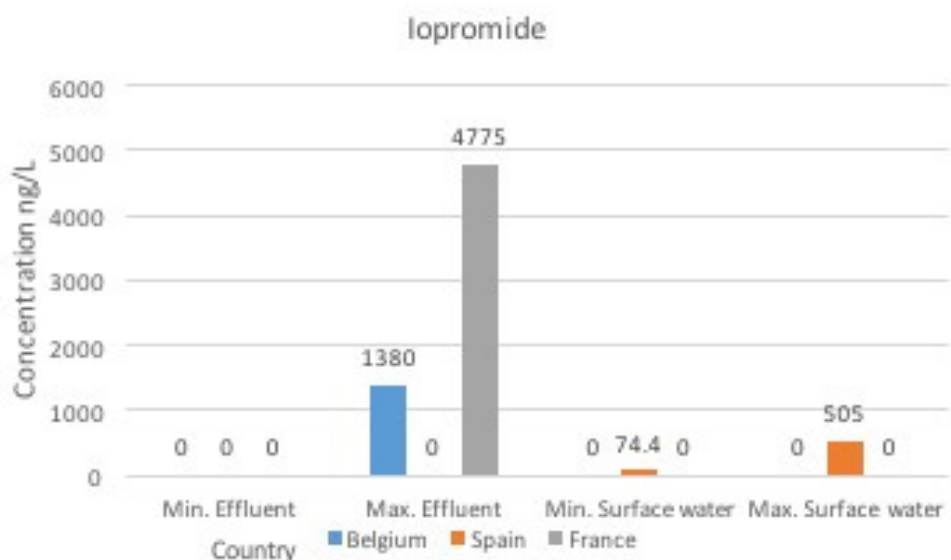


Figure 4: Occurrence and concentration of iopromide in effluent and surface water around world 2006-2013

Figure 3 shows the range of iopromide concentration founded in the research in different areas of the world. Concentration zero means not reported.

Iopromide was reported in relatively fewer countries. The concentration of iopromide in effluent was much higher than in the surface water. France, the highest concentration reported was 4775 ng/L.

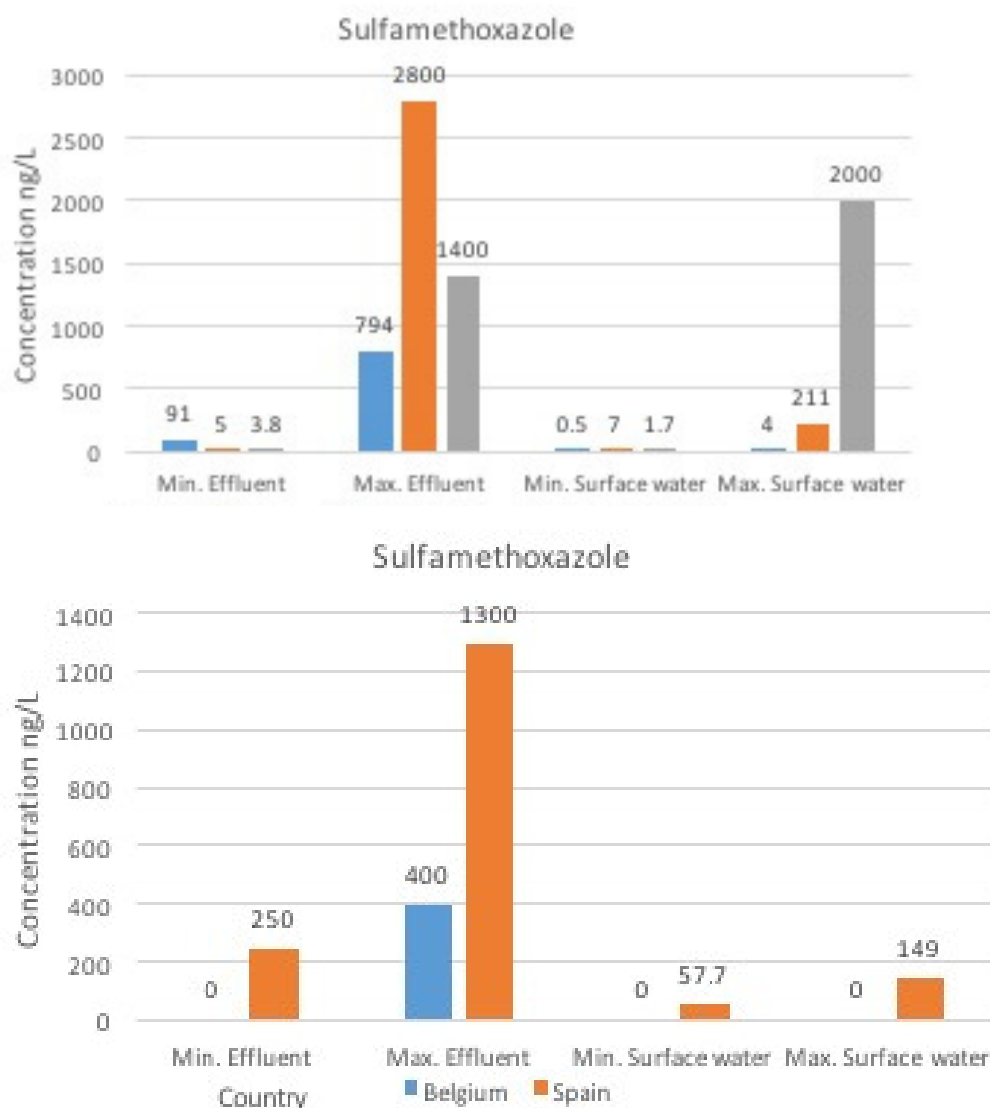


Figure 5: Occurrence and concentration of sulfamethoxazole in effluent and surface water around world 2006-2013

Figure 5 shows the range of sulfamethoxazole concentration founded in the research in different area. Concentration zero means not reported. Sulfamethoxazole was widely existed in the world. Diclofenac concentration in effluent was reported between 5 ng/L to 2800 ng/L in North America, 91 ng/L to 794 ng/L in Europe, and 3.8 ng/L to 1400 ng/L in Asia and Australia. It was 7 ng/L to 211 ng/L in North America, 0.5 ng/L to 41 ng/L in Europe, and 1.7 ng/L to 2000 ng/L in Asia and Australia in surface water. It was not reported in surface water Belgium and the highest in surface water was 103.35 ng/L in Spain.

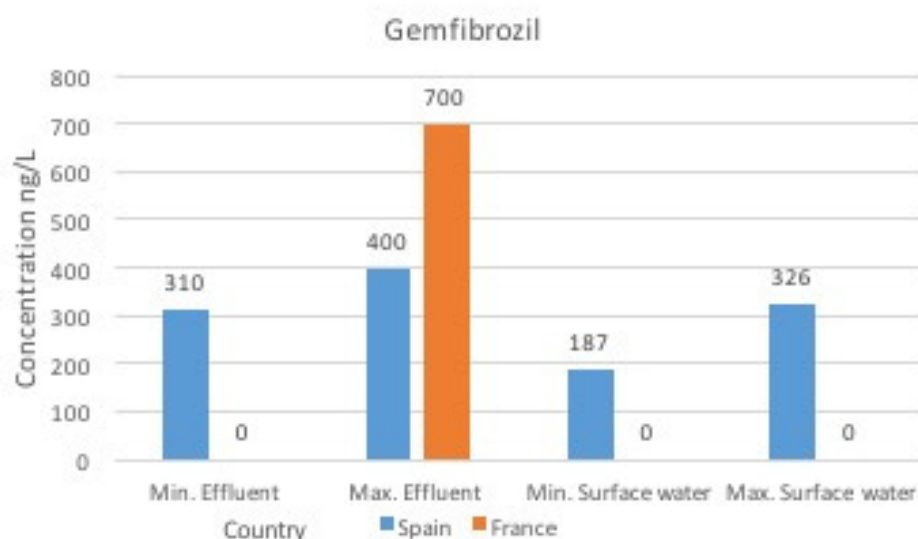
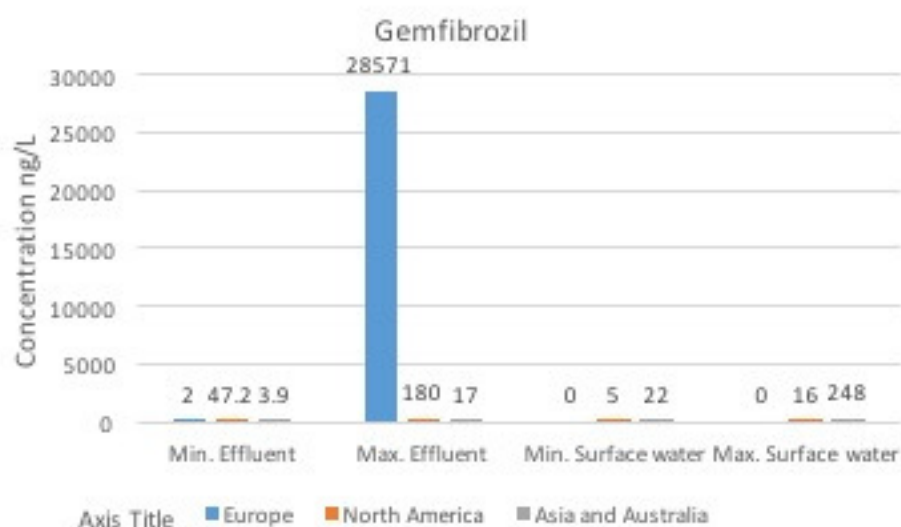


Figure 6: Occurrence and concentration of gemfibrozil in effluent and surface water around world 2006-2013

In Figure 6 the range of gemfibrozil concentration founded in the research in different area is shown. Concentration zero means not reported. Gemfibrozil in surface water was much lower than in effluent. Many places were not reported in surface water like France and Mexico. Gemfibrozil concentration in effluent was reported between 47.2 ng/L to 180 ng/L in North America, 2 ng/L to 28571 ng/L in Europe, and 3.9 ng/L to 17 ng/L in Asia and Australia. It was 5.4 ng/L to 16 ng/L in North America and 22 ng/L to 248 ng/L in Asia and Australia in surface water.

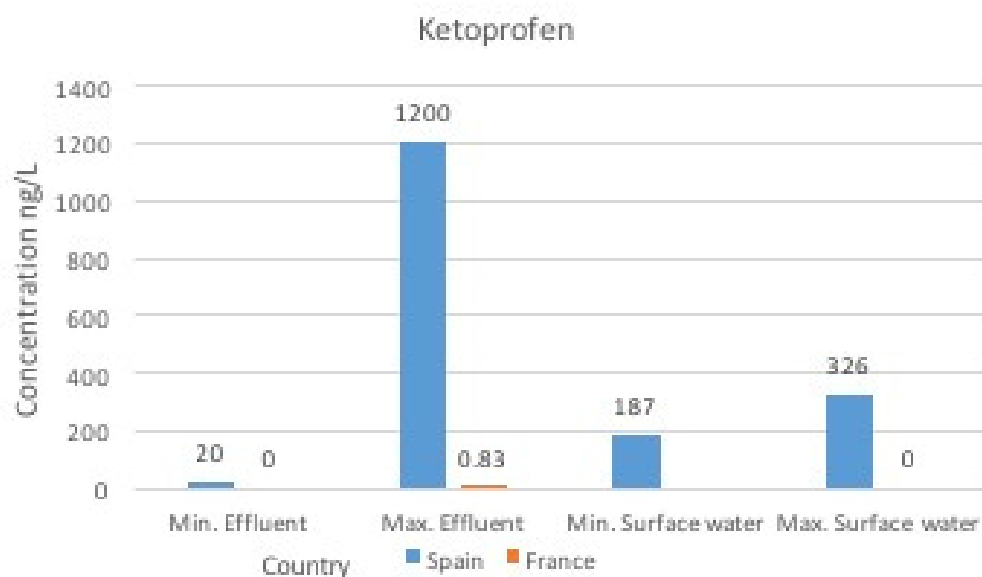
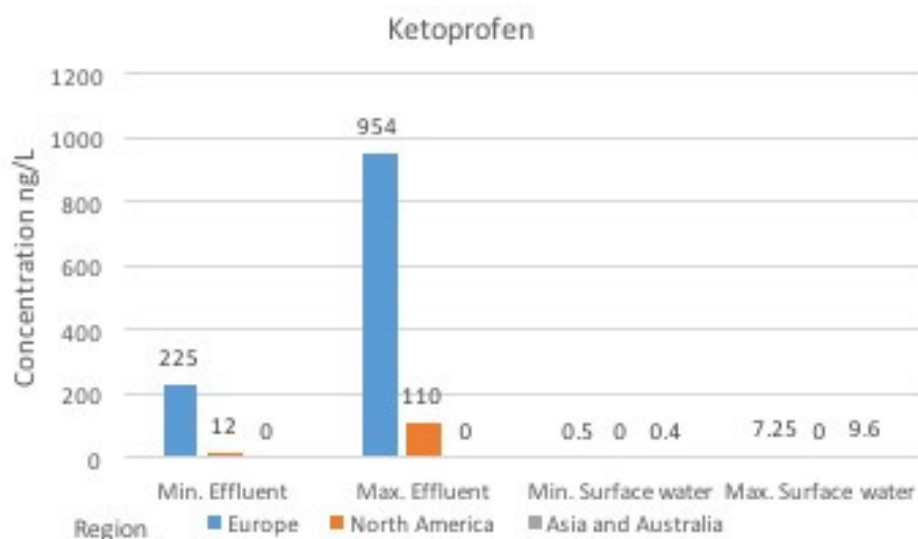


Figure 7: Occurrence and concentration of ketoprofen in effluent and surface water around world 2006-2013

Figure 7 shows the range of ketoprofen concentration founded in the research in different area. Concentration zero means not reported. Ketoprofen in the surface water was very low and not reported in many places such as Spain, France and Mexico. In effluent, the highest concentration was in Spain 590 ng/L and in Europe 954 ng/L.

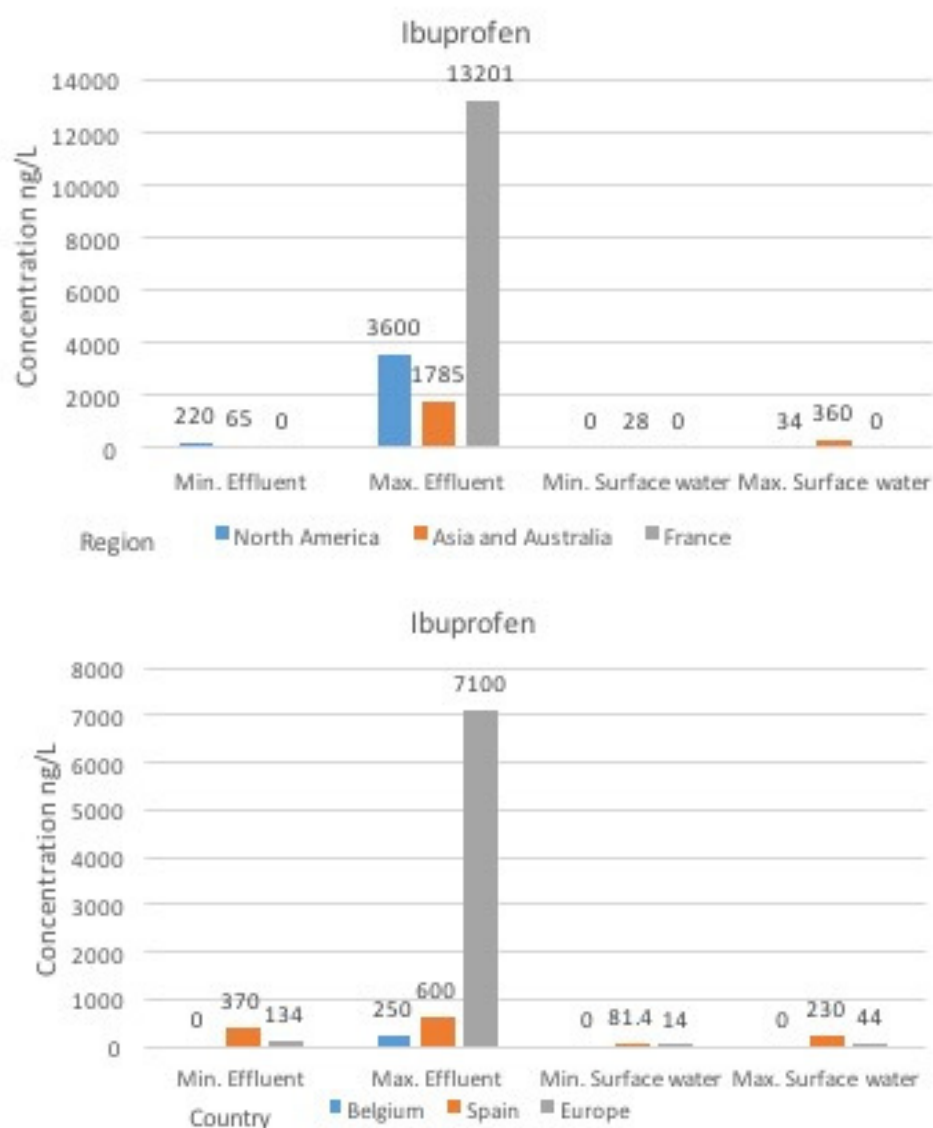


Figure 8: Occurrence and concentration of ibuprofen in effluent and surface water around world 2006-2013

The range in Figure 8.. Concentration zero means not reported. m

Ibuprofen widely exists in the world. Its concentration in effluent was relatively higher compared to other PPCPs. Ibuprofen concentration in effluent was reported between 220 ng/L to 3600 ng/L in North America, 134 ng/L to 7100 ng/L in Europe, and 65 ng/L to 1785 ng/L in Asia and Australia. But the concentration of ibuprofen was much lower in surface water. It was zero ng/L to 34 ng/L in North America, 14 ng/L to 44 ng/L in Europe, and 28 ng/L to 360 ng/L in Asia and Australia in surface water. It was not reported in the surface water of Belgium and France.

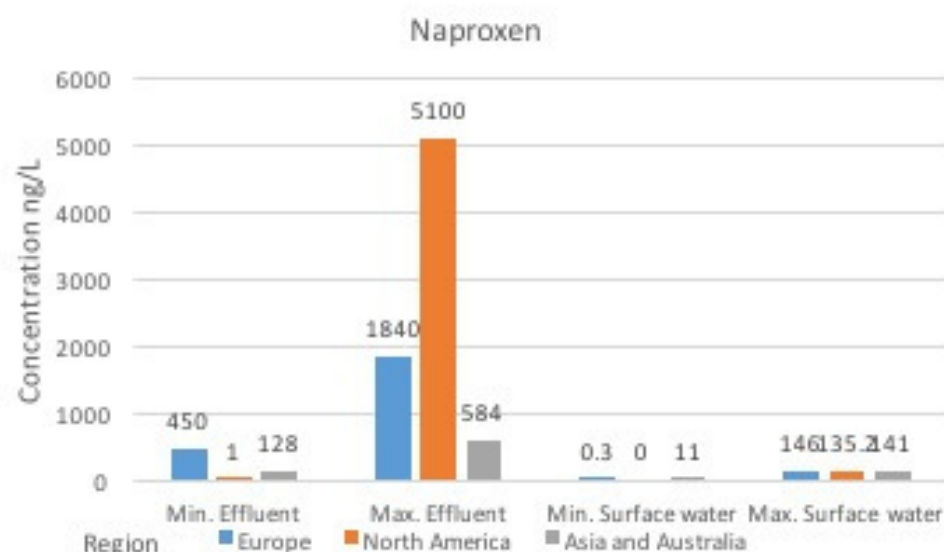
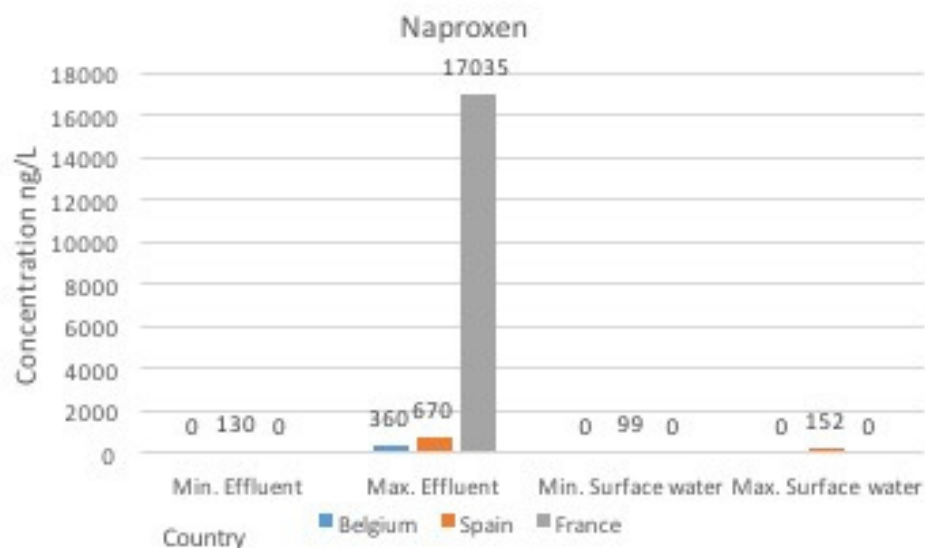


Figure 9: Occurrence and concentration of naproxen in effluent and surface water around world 2006-2013

Figure 9 shows the range of naproxen concentration founded in the research in different area. Concentration zero means not reported. Naproxen concentration in effluent was reported between 1 ng/L to 5100 ng/L in North America, 450 ng/L to 1840 ng/L in Europe, and zero ng/L to 135.2 ng/L in Asia and Australia. The highest concentration detected in effluent in France 17035 ng/L. But the concentration of naproxen was much lower in surface water. It was zero ng/L to 34 ng/L in North America, 0.3 ng/L to 146 ng/L in Europe, and 11 ng/L to 181 ng/L in Asia and Australia in surface water. In effluent of US, in surface water of Belgium it was not reported.

4. TREATMENT TECHNOLOGIES FOR REMOVAL OF PPCPS

Traditionally treatment processes are not designed to remove the trace amount PPCPs. New methods and technologies should be applied to treat the wastewater containing such substances.

4.1 Physicochemical treatment

Physicochemical treatment as a coagulation–flocculation process was generally found to be unable to effectively remove PPCPs. Addition of activated carbon power, water treatment by chlorination and ozonation can be more effective to remove PPCPs. In 2005, a study conducted by Westerhoff *et al.* [30], using a bench-scale simulation water treatment plant model and natural waters spiked with 30 pharmaceuticals to 80 different Endocrine disruptors (EDCs) to test the removal efficiency by different treatment processes. 90% of the PPCPs and EDCs were removed through chlorination and ozonation. 50-98% of PPCPs and EDCs were removed by adding 5ml/L powder activated carbon for a four-hour contacting. The treatment processes like coagulation and chemical lime softening only remove less than 25% of the PPCPs and EDCs. Table 2.3 shows the results for removal performance with different processes.

Table 2: Removal performance of EDCs by selected treatment processes

Treatment process	Removal performance
Coagulation Add aluminum sulfate and ferric chloride as coagulant	<25% of EDCs/PPCPs removed
Chemical lime softening Add calcium hydroxide and soda ash simulated chemical softening treatments	<25% of EDCs/PPCPs removed
Powder activated carbon (PAC) 5 mg/L of (PAC) with a 4-h contact time.	50-98% removed Higher PAC dosages improved EDC/PPCP removal
Chlorination Add 1200 mg/L chlorine solution	Able to remove >90% for more reactive compounds containing aromatic structures with hydroxide functional groups Not suitable because it produces chlorine by-product.
Ozonation Add 40-50 mg O ₃ / L liquid ozone solution	Oxidized methods is similar to chlorination but at slightly higher removal rates Addition of hydrogen peroxide during ozone addition slightly increased the EDCs/PPCPs removal.

4.2 Biological treatment

Biological treatment removes only a part of a wide range of PPCPs, while some of them are much more resilient to degradation especially, polar ones which are discharged with the effluent [3], [19]. In 2005, Urase and Kikuta [31] tested the removal of 10 PPCPs like ibuprofen by activated sludge. At the neutral pH condition, PPCPs showed little tendency for adsorption in the sludge because they appeared as ions and remained in the water phase. While there is an increasing tendency of absorption observed in the lower pH conditions, biological treatment was weak because the limiting stage for removal was not biodegradation, but the transfer of substances from the water phase to the sludge phase.

4.3 Advanced treatments

Advanced treatment for removing PPCPs include ultra-violet (UV) photolysis, ion exchange and membrane filtration [32]

UV and ion-exchange can improve the removal of PPCPs, but they were insufficient to be considered as feasible removal options for future application because the removal efficiency was depending on the dosages: the higher the better [13], [33]. Membrane filtration technology such as reverse osmosis (RO), or Nano-filtration (NF) has demonstrated itself as a promising alternative for eliminating micro-pollutants [32].

In the study of Urtiaga [34], the Ultrafiltration (UF) removal efficiency was less than 20% for the majority of the micro-pollutants,. Excellent removal efficiencies were achieved with the RO treatment.

4.4 Constructed wetlands

Constructed wetlands (CWs) for wastewater treatment were engineered designed, constructed to utilize natural processes. They mimic natural wetland systems, utilizing wetland plants, soil, and associated microorganisms to remove contaminants (Like solids, nitrogen, phosphorous, heavy metals, etc.) from wastewater effluents [35].

But with the more concern of PPCPs, CWs are also improved for removing PPCPs. Matamoros and Bayona [36] used subsurface horizontal flow constructed wetlands (SSFWs) to remove he PPCPs, and found that caffeine, salicylic acid, methyl dihydrojasmonate, and carboxyl-ibuprofen were 80% removed, ibuprofen, hydroxy-ibuprofen, and naproxen were 50–80% removed, ketoprofen and diclofenac were difficult to remove. A similar study conducted by Matamoros et al. at 2007 [37] using vertical subsurface-flow constructed wetland (VFCW). Caffeine, salicylic acid, methyl dihydrojasmonate, CA-ibuprofen, hydrocinnamic acid, oxybenzone, ibuprofen, and OH-ibuprofen were more than 95% removed, naproxen, diclofenac, galaxolide, and tonalide were 70 to 90% removed, and carbamazepine were less than 30% removed.

Prado Wetlands, covering 425 acres located at southern California. In 2004, a study [38] of these wetlands found that the site helped reduce levels of ibuprofen and organic chemicals found in pesticides and flame retardants. And new project [39] was conducted at Prado Wetlands channels river water through three ponds. Sunlight and bacteria are used to degrade residues of antibiotics, anti-inflammatories, sex hormones, and other drugs and man-made chemicals.

5. FUTURE WORK AND DIRECTIONS

More studies should be done on PPCPs' risks on human since these risks to humans in both short-term and long-term exposure at low concentration remain poorly understood [5].

Study more of the fate of the PPCPs through animals, plants or even human bodies.

Build a more complete environmental monitoring system to collecting the data and track the these PPCPs, globally if possible.

6. CONCLUDING REMARKS

In this review, PPCPs are widely exist around world at trace level. Some regions show very high level of one or two PPCPs such as Carbamazepine in Belgium, Trimethoprim in North America. Currently there are many useful techniques for the analysis of PPCPs, for instance, GC/MS, LC-MS/MS, HPLC/UV and UPLC/MS/MS. And EPA uses a high-performance liquid chromatography combined with tandem mass spectrometry (HPLC/MS/MS) method. For removing the PPCPs in the surface and wastewater, conventional physicochemical treatment as a coagulation–flocculation process is not efficient enough. While some advanced techniques like reverse osmosis (RO), nano-filtration (NF) and constructed showed great removal efficiency in studies and in the application of many regions.

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