Available online at www.jobpcr.com

ISSN-2394:3076
CODEN(USA) : JBPCBK

Journal of Biological Pharmaceutical And Chemical Research , 2015,2(1):13-20

(*http://www.jobpcr.com/arhcive.php*)

PHARMACEUTICALS IN THE ENVIRONMENT

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ABSTRACT

Pharmaceuticals are natural or artificial substances. Their presence in the environment is an important issue, because multiple studies have shown that pharmaceuticals are present in water bodies used for production of drinking water and in some cases even in tap water.

It is important to examine the ways how they get into the environment and the risk of short term or long term exposition to them.

Keywords : Pharmaceuticals, Drinking Water Treatment, Environment

INTRODUCTION

The pharmaceuticals are artificial or natural substances, which are supposed to positively affect health of humans and animals. They have pharmaceutical and immunological effect, or they caninfluence the metabolism. Pharmaceuticals are compounds of chemical, plant or animal origin. [1]

Presence of pharmaceuticals in natural environment has become an important issue in last years. It concerns both the professional and non-professional public. Many articles and studies focusing on potential risks of their presence in the environment have been written. Most studies were written in the USA and Germany.

Reason for this attention is in the fact that the consumption of pharmaceuticals is increasing. Millions of packages of various pharmaceuticals are used daily. These pharmaceuticals contain over 300 different active ingredients. Most frequently used pharmaceuticals are antibiotics, antidepressants, synthetic hormones, nutraceuticals, cytostatics, beta – blockers. [2]

Another reason for increased attention to presence of pharmaceuticals in the environment is that these substances are present in natural water bodies. That fact is partly because of advance of analytical technologies.

MATERIALS AND METHOD

Studies and articles concerning presence of pharmaceuticals in the environment

First reports about presence of pharmaceuticals in the environment are from the 1970s. First significant report was published in 1993 (Heberer et al.). It was about finding high concentration (more than 165 ng/l) of clofibric acid in water taps in Berlin. [7]

Since that time many works and projects were done on that topic. Here are some of these projects:
Project KNAPPE (Knowledge and Need Assessment on Pharmaceutical Products in Environmental Waters)
KNAPPE Project was financed by the European DG Research (in a frame of the 6FP) to make the state of the art of the current knowledge in this topic in order to identify the main gaps and answer several questions deserving attention such as:

- What is the list of most relevant pharmaceuticals (PPs) in terms of exposure for the aquatic environment?
- What is the efficiency of urban and industrial sewage treatment plants over a year? What is the fate and behaviour of PPs in sewage treatment plants? If receiving waters are used for potable water supplies, does the presence of these compounds represent a potential hazard to human health?
- Could we solve some problems by environmental or cleaner technologies?

KNAPPE project has initiated discussions through workshops and conferences with the concerned groups of experts (pharmaceutical industry, water managers, healthcare community, patients and regulatory institutions) and provide the information to all stakeholders by means of the maximum readable ways. [13]

Project Poseidon (EU): Main goal is the assessment of technologies for the removal of pharmaceuticals and personal care products in sewage and drinking water facilities to improve the indirect potable water reuse. POSEIDON develops methods which will reduce the uncontrolled releases of PPCPs to the environment via wastewater. [14]

Pharmaceuticals in the environment (PEIAR)
It is a website with database of available information on the general chemistry and toxicology of potential environmental levels of pharmaceuticals. The database is managed by National Centre for Coastal Ocean Science (NCCOS).

The database provides information on prescribed amounts, levels detected in aquatic environments, chemical structure, molecular weight, octanol-water partition coefficients, water solubility, environmental persistence, general toxicity information and specific toxicity levels to five groups of organisms (algae, molluscs, finfish, crustaceans, and select terrestrial animals). [11]

Tab. 1 *Table exported from PEIAR database, hormone drugs according to aquatic organism toxicity. [11]*

Toxicity		ID	Toxicity type	CAS Number	Active Ingredient	Species	Species (Sci.)
> 10	mg/	30		50-28-2	Estradiol	Copepod	Acartia

	l						tonsa
0.0000014 - 0.00000203	mg/l	146	LD50	57-63-6	Ethinyl Estradiol	Sheepshead minnow	Cyprinodon variegatus
0.0000804	mg/l	150	LD50	58-18-4	Methyl-testosterone	Alaskan sickleback	Gasterosteus aculeatus
0.0187	mg/l	30		50-28-2	Estradiol	Mimmichog	Fundulus heteroclitus
0.51	mg/l	146	LD50	57-63-6	Ethinyl Estradiol	Harpacticoid copepod	Nitocra spinipes

Issue of presence of the pharmaceuticals in the environment was added to the work plan of the World Health Organization (WHO) Drinking-water Quality Committee in 2005. It was proposed that a working group of experts will be assembled to undertake a rapid review of the state of the science of pharmaceuticals in drinking-water and develop guidance and recommendations in a report and fact sheet.

A WHO working group that comprised experts in toxicology, water chemistry, water quality and health, water treatment, pharmacology, and drinking-water regulation and policy was formed in 2009. Consultations were held in 2009 and 2010 with the Drinking-water Quality Committee and additional experts review and summarize the available scientific knowledge and evidence.

Outcomes from this working group can be found in directives for drinking water quality (for example report from 4.2011). Low concentrations of PPs in tap water have been found in countries like The USA, Germany, Italy and Netherlands.

Therefore the group recommends to concentrate future studies on long-term exposal of human organism to low concentrations of PPs in drinking water. [8]

In the Czech Republic the first articles on that topic started to appear in 2002. Therefore the National Health Institute in Prague decided to pay more attention to this problem. They prepared a project which in years 2009 – 2011 carried out a wide screening, focused on presence of the pharmaceuticals in drinking water. The goal of this project was to evaluate human exposition to the PPs in drinking water and health risks resulting from it.

The samples have been collected from public water mains covering all regions of the Czech Republic. Most samples were originally taken from surface water sources (90%) and the rest from groundwater sources. 5 substances were chosen to be observed: Carbamazepin, Naproxen, Ibuprofen, Diclofenac, Ethinylestradiol.[7]

Measurements were conducted in three steps. Firstly basic representative screening was done, than the samples from critical localities were taken. Third step was verification of higher concentrations of the substances which were found in second step.

Samples were taken from more than 100 water mains. Positive findings were only in 4 cases. Three times it was ibuprofen (0,5 – 1,2 ng/l), and once carbamazepin (4,0 ng/l).

This positive outcome is mainly due to the structure of water delivery in the Czech Republic because most of the surface water is taken from protected water basins and there is also a big amount of ground water sources. [17]

Entry and presence in the environment

Most frequent sources of pharmaceuticals in the environment are:

- Human activity
- Residues from pharmaceutical manufacturing (well defined and controlled)
- Residues from hospitals
- Illicit drugs
- Veterinary drug use, especially antibiotics and steroids
- Agribusiness

The main source of the pharmaceuticals and their metabolites in the environment are the patients in the hospitals or women using birth control pills. After usage of the drug active ingredients are excreted from the body either unchanged or in a form of metabolites. The pathway to the environment typically is with the waste stream – domestic wastewater (via septic systems or wastewater treatment plants), domestic solid wastes (via landfill leakage).

Other sources are the pharmaceuticals over their guarantee period which are threw away from the household. People get rid of them by flushing them into a toilet or throwing them away with the garbage. These pharmaceuticals can reach to the groundwater via landfill leakage. According to some researches over two thirds of these pharmaceuticals end up with the garbage, and one fifth gets into the sewage water. [6]

An obvious source for PPs as environmental pollutants includes residues from their manufacturing. But the discharges of pharmaceuticals and synthesis materials and by-products from manufacturing are already well controlled so the loss of the PPs during manufacturing is very small because of that.

Except for human pharmaceuticals there are also pharmaceuticals for the animals which contribute to their presence in the environment. Among them belong the pharmaceuticals, which are used for animal agriculture and also those which are use in animal agriculture (such as animal feeding operations) or in veterinary medicine (healing pets)

Direct source of pharmaceutical pollution is from fish breeding, because these pharmaceuticals are added directly into the water and so to the environment. [9,12]

Summary of Fate and transport of pharmaceuticals in the environment is in Image 1:

The pharmaceuticals can be also naturally removed from the environment, but only in very small amounts and with low efficiency. The natural ways of their removal are photodegradation, biodegradation a bank filtration. [2,3]

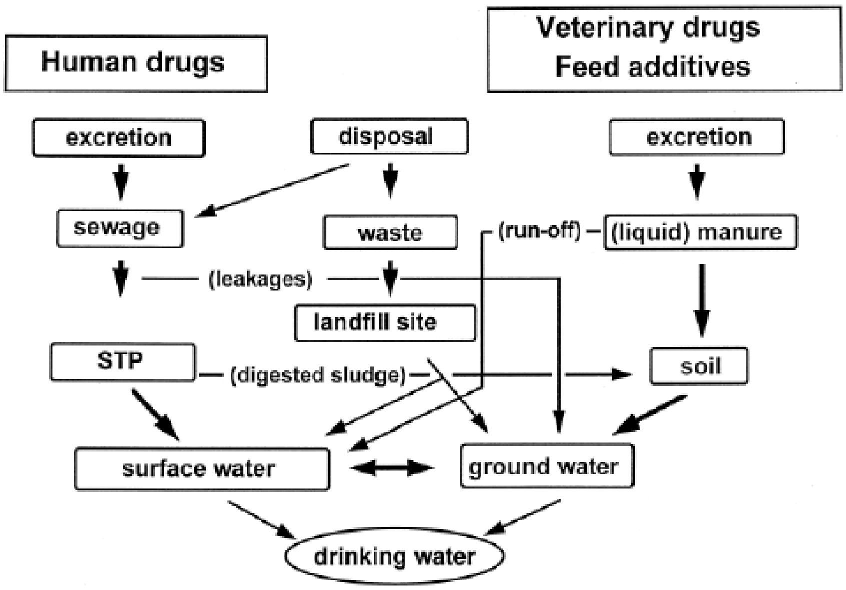

Fig. 1 - Fate and transport of pharmaceuticals in the environment (Ternes, 1998)

Waste water treatment technologies for removal of pharmaceuticals

Conventional wastewater treatment facilities generally have activated sludge processes or other forms of biological treatment such as biofiltration. These processes have demonstrated varying removal rates for pharmaceuticals, ranging from less than 20% to greater than 90%. The efficiency of these processes for the removal of pharmaceuticals varies within and between studies and is dependent on operational configuration of the wastewater treatment facility. Factors influencing removal include sludge age, activated sludge tank temperature and hydraulic retention time.

Comparatively, advanced wastewater treatment processes, such as reverse osmosis, ozonization and advanced oxidation technologies, can achieve higher removal rates for pharmaceuticals. There has been an extensive study focusing on impact of water ozonization on PPs by Snyder and col. They proved that ozonization can remove most types of PPs (for ex.: Paracetamol)
Besides these methods we can also use membrane separation processes or sorption on activated carbon. [6]

The issue with PPs in surface water is not only that it can affect water organisms (sex changes of fishes due to estrogen in waters) but it also can enter waters which are used as a source for drinking water Studies from a team of scientists discovered the presence of estrogens in Želivka basin (Morteani et al., 2004), which is Prague's major drinking water source. Estimated concentrations of discovered substances were about 2 ngl^{-1} [2, 4, 6]

Drinking water treatment technologies for removal of pharmaceuticals from raw water

Studies on conventional drinking-water treatment processes have shown that coagulation is largely ineffective in removing pharmaceuticals. Free chlorine is able to remove up to approximately 50% of the pharmaceuticals investigated, whereas chloramines have lower removal efficiency.

Advanced water treatment processes, such as ozonization, advanced oxidation, activated carbon and membranes (e.g. nanofiltration, reverse osmosis), are able to achieve higher removal rates (above 99%) for targeted pharmaceutical compounds.[2]

Ozonization is usually used when organic compounds are removed. These compounds cause problems with colour and smell of water. [5]

Activated carbon is mostly used to remove dissolved organic compounds of polar character. The great advantage of this process is that there are almost no harmful byproducts. It has also proved to be very efficient way to remove karbamazepin which survives most of others treatment processes. Disadvantage is that the efficiency of sorption processes is decreasing if another organic compounds are involved in treatment processes. [2,5,6]

Membrane processes such as reverse osmosis and nanofiltration are also effective, but their usage isn´t recommended for drinking water if it is not necessary. If we use them we must remineralise the water. [5,15]

Factual study focused on removal of the pharmaceuticals in water treatment processes

In article: „*Occurrence and removal of pharmaceuticals and hormones through drinking water treatment“ from Maria Huerta-Fontela, Maria Teresa Galceran a Francesco Ventura*, the occurrence of fifty-five pharmaceuticals, hormones and metabolites in raw waters used for drinking water production and their removal through a drinking water treatment were studied. Thirty-five out of fifty-five drugs were detected in the raw water at the facility intake with concentrations up to 1200 ng/L. The behaviour of the compounds was studied at each step of water treatment process.

The raw water used for drinking water production consists of surface water from the Llobregat River (NE-Spain) which exhibits a highly variable quality. [7]

The intake water enters into the Drinking water treatment plant (DWTP) at flow rates ranging from 2300 to 5100 L/s. First, chlorine is added until break-point is achieved and then several coagulants (i.e. $Al_2(SO_4)_3$, $Al_x Cl_3$, Al_2O_3) and flocculants (poly-DADMAC) are also added. Clarified water passes through sand filters (0.60m height; 15-30 min) and at this point dilution with groundwater from the aquifer is performed at variable percentages (6-29%) to improve the water quality. The water is then pumped to ozone treatment facilities. Ozone is generated in situ and water is treated inside of four ozone chambers (5 mg/L for nominal flow), yielding a residual concentration of 0.2 mg/L. This treatment lasts around 15-20 min depending on the treated water volume. The water is then passed through GAC filters (10 m/h) for at least 15 min at a water flow rate of $6m^3/s$. Finally, a post-chlorination step is performed in order to maintain a chlorine residual concentration of about 70.8-1.2 mg/L when leaving the DWTP [7]

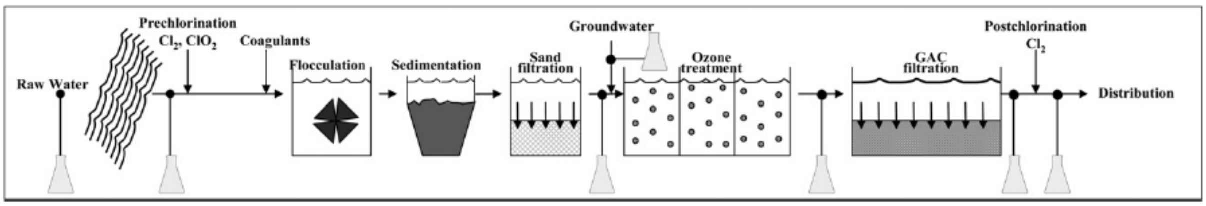

Fig. 2 - Treatment scheme of the DWTP and location of sampling points **[7]**

Five pharmaceuticals out the 55 selected in this study survived treatments and were found in finished waters at trace levels: phenytoin, atenolol, sotalol, hydrochlorothiazide and carbamazepine. [7]

Coagulation, flocculation and sand filtration showed, in general, poor removal efficiencies, while chlorination and ozonization accounted for the higher efficiencies. Both oxidation processes removed a high number of contaminants found in raw waters, above 20 out of 35 compounds found at raw waters. GAC filtration was also efficient to remove compounds with high hydrophobic properties while dilution with groundwater demonstrated to be inadequate for some pharmaceuticals due to their presence in these matrices. [7]

CONCLUSION

The occurrence of human pharmaceuticals and endocrine disrupting compounds (EDCs) in wastewaters and in surface waters; has been demonstrated and widely evaluated in the last decade. These compounds together with their metabolites enter the environment primarily through sewage treatment plants.

The relatively recent awareness of pharmaceutical products (PPs) impact on environment is reflected in literature since the 1990s through the exponentially increasing number of studies concerning this emergent class of water pollutants.
The great majority of studies on pharmaceutical products PPs in water concerns their analysis, occurrence and fate in wastewaters (WW) and wastewater treatment plants (WWTP), with an emphasis on processes efficiency with respect to their removal.
Only few studies are concerning the problem of their occurrence in tap water.
It is important to check the absence of the most widespread PPs in the main drinking water networks. Furthermore there is a real need for complementary studies such as the comparison on PPs consumption and occurrence in water based on a reference methodology, or the identification and toxicity assessment on the degradation Byproducts formed during drinking water treatment. Another important aspect, to which we should pay attention and study it, is the long-term effect of low concentrations of these substances on the human body.

ACKNOWLEDGMENT

This research has been supported by SGS grant SGS 13/172/OHK1/3T/11.

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