



ECOTOXICITY OF WASTEWATER FROM MEDICAL FACILITIES: A REVIEW*

A. Cidlinová^{1,2}, Z. Wittlingerová¹, M. Zimová^{1,2}, T. Chrobáková¹, A. Petruželková¹

¹*Czech University of Life Sciences Prague, Faculty of Environmental Sciences, Prague, Czech Republic*

²*The National Institute of Public Health, Prague, Czech Republic*

Wastewater from medical facilities contains a wide range of chemicals (in particular pharmaceuticals, disinfectants, heavy metals, contrast media, and radionuclides) and pathogens, therefore it constitutes a risk to the environment and human health. Many micropollutants are not efficiently eliminated during wastewater treatment and contaminate both surface water and groundwater. As we lack information about the long-term effects of low concentrations of micropollutants in the aquatic environment, it is not possible to rule out their adverse effects on aquatic organisms and human health. It is, therefore, necessary to focus on the evaluation of chronic toxicity in particular when assessing the environmental and health risks and to develop standards for the regulation of hazardous substances in wastewater from medical facilities on the basis of collected data. Wastewater from medical facilities is a complex mixture of many compounds that may have synergetic, antagonistic or additive effects on organisms. To evaluate the influence of a wide range of pollutants contained in the effluents from medical facilities on aquatic ecosystems, it is necessary to determine their ecotoxicity.

hospital wastewater, health and environmental risks, pharmaceuticals



doi: 10.2478/sab-2018-0005

Received for publication on November 10, 2016

Accepted for publication on September 7, 2017

INTRODUCTION

Wastewater from medical facilities constitutes, given the large quantities of substances contained, three types of risk: toxic, infectious, and radioactive (Panouilleres et al., 2007). It is estimated that it is 5 to 15 times more toxic than municipal sewage (Emmanuel et al., 2009). The toxic effects of substances contained in wastewater are often observed on the organisms for which no such substances were primarily intended (Zgorzka et al., 2011).

Wastewater from medical facilities is usually released without pretreatment directly into the sewage

system. Although the major part of wastewater from medical facilities is only a small fraction of the total volume of wastewater entering the wastewater treatment plants, it is being given more and more attention by both scientists and the public (Ort et al., 2010).

The aim of this work was to review the current knowledge about the ecotoxicity of wastewater from medical facilities and to draw attention to the risks to the environment and human health posed by such wastewater and contained substances.

Verlicchi et al. (2010) quote the following average concentrations of major groups of micropollutants in effluents from medical facilities and in

* Supported by the Internal Grant Agency of the Faculty of Environmental Sciences, Czech University of Life Sciences Prague, Project No. 20154235.

municipal wastewater: concentration of analgesics ($100 \text{ mg l}^{-1}/11.9 \text{ mg l}^{-1}$), antibiotics ($11 \text{ mg l}^{-1}/1.17 \text{ mg l}^{-1}$), cytostatic agents ($24 \text{ mg l}^{-1}/2.97 \text{ mg l}^{-1}$), β -blockers ($5.9 \text{ mg l}^{-1}/3.21 \text{ mg l}^{-1}$), hormones ($0.16 \text{ mg l}^{-1}/0.10 \text{ mg l}^{-1}$), iodinated contrast media ($1008 \text{ mg l}^{-1}/6.99 \text{ mg l}^{-1}$), adsorbable organic halogens – AOX ($1371 \text{ mg l}^{-1}/150 \text{ mg l}^{-1}$), gadolinium ($32 \text{ mg l}^{-1}/0.7 \text{ mg l}^{-1}$), platinum ($13 \text{ mg l}^{-1}/0.155 \text{ mg l}^{-1}$), and mercury ($1.65 \text{ mg l}^{-1}/0.54 \text{ mg l}^{-1}$). From the above it can be seen that the average concentration of pollutants in wastewater from medical facilities is approximately 2 times up to 150 times higher than that in municipal wastewater.

The treatment of wastewater from medical facilities

Common scenarios for the treatment of wastewater from medical facilities are according to Pauwels, Verstraete (2006) as follows:

- (1) draining wastewater into the sewage system and treating in the municipal wastewater treatment plant,
- (2) on-site wastewater treatment in the hospital treatment plant and draining the treated wastewater into the environment,
- (3) on-site wastewater treatment in the hospital treatment plant and subsequent purification in the municipal wastewater treatment plant.

And, unfortunately, in some cases wastewater from medical facilities is not treated at all and is discharged directly into the environment. This is the situation especially in underdeveloped countries.

Despite its specific nature, wastewater from medical facilities is frequently discharged into the public sewage system and treated together with municipal wastewater (Ternes, Joss, 2006; Verlicchi et al., 2010). This solution, based on the dilution of pollutants emitted, is considered insufficient by many researchers (e.g. Pauwels, Verstraete, 2006; Gautam et al., 2007; Vieno et al., 2007), because it does not allow the segregation/separation of pollutants, which are then discharged into the environment.

Municipal wastewater treatment plants are designed for the elimination of carbon, nitrogen, and phosphorus compounds and microorganisms from wastewater, but are not efficient for the removal of micropollutants (particularly the pharmaceuticals). This is complicated by their very low concentrations (10^{-3} to $10^{-6} \text{ mg l}^{-1}$) in comparison with the concentration of normal macropollutants (organic contamination measured using BOD_5 – biochemical oxygen demand, COD – chemical oxygen demand, compounds of nitrogen, phosphorus, etc.) (Verlicchi et al., 2010).

However, a separate treatment of wastewater from medical facilities is not supported unanimously either as many pharmaceuticals are used also in households on a regular basis. Schuster et al. (2008) consider separate treatment of hospital wastewater not enough effective. They assume that such a process would capture only a small part of active pharmaceutical

compounds and at the same time would lead to high costs. On the contrary, according to the European Community Directive 2013/39/EU, the issue of emissions of pollutants should be addressed at source, in a both economically and environmentally effective manner.

Kummerer (2009) questions the influence of separate treatment of wastewater from medical facilities on reducing the bacterial resistance development as bacteria resistant to antibiotics are also very common in wastewater outside hospitals.

The risks associated with wastewater from medical facilities

Several research groups were involved in the assessment of environmental risks posed by selected pharmaceuticals contained in the effluents from medical facilities for both the environment and human health (Escher et al., 2011; Verlicchi et al., 2012; Al Aukidy et al., 2014; Orias, Perrodin, 2014). The risk posed by pharmaceuticals depends not only on their concentration in effluents, but also on their ecotoxicity. Therefore, Orias, Perrodin (2014) assessed the hazard quotient (HQ) for 127 pharmaceuticals using their highest measured concentration in effluents from medical facilities, divided by the Predicted No-Effect Concentration (PNEC). The PNEC values for individual pharmaceuticals determined in this study were in the range from 0.05 pg ml^{-1} (for clotrimazole) to 45.7 mg l^{-1} (for iohexol). For 50 pharmaceuticals the prescribed HQ values were lower than 1, for 62 pharmaceuticals the HQ values were in the range from 1 to 1000, and for 15 pharmaceuticals (ampicillin, clotrimazole, 5-fluorouracil, 17β -estradiol, norfloxacin, 17α -ethinylestradiol, chlorpromazine, diclofenac, lidocaine, estrone, trimethoprim, sulfapyridine, ofloxacin, sulpiride, and propyphenazone) the determined HQ was higher than 1000. According to the classification used in many studies (e.g. Verlicchi et al., 2012; Santos et al., 2013) the risk is classified as high ($\text{HQ} \geq 1$), medium ($1 > \text{HQ} > 0.1$), and low ($\text{HQ} \leq 0.1$). Diclofenac, 17β -estradiol, and 17α -ethinylestradiol were included in the first European list of substances monitored in order to collect data facilitating the establishment of appropriate measures to address the risks that these substances constitute (European Community Directive 2013/39/EU).

Acute toxic effects of low concentrations of pharmaceuticals in the environment are not likely, but due to the lack of information, it is not possible to exclude adverse effects resulting from the long-term impact of low doses of pharmaceuticals. Recently, for example, the disturbance of the fish endocrine system caused by the effect of traces of contraceptive substances in rivers has been proven (Kostich, Lazorchak, 2008). The ethylestradiol concentration of 10 ng l^{-1}

caused damage to larval structure of mouthpart of *Chironomus riparius* (Watts et al., 2003) and that of 100 ng l⁻¹ caused the change of the female to male ratio from 1 : 1 to 2 : 1 in the population of *Gammarus pulex* (Watts et al., 2002).

The health risks associated with the consumption of pharmaceuticals in drinking water are considered unimportant because the maximum intake of pharmaceuticals in drinking water during the whole life is significantly lower than the treatment dose (Kummerer, 2009). The influence of pharmaceuticals in drinking water on the high-risk groups (elderly people, children, and people with impaired renal function and liver) cannot be entirely ruled out (Kostich, Lazorchak, 2008). It is also suspected that the cytostatic agents contained in wastewater may be the cause of the increased number of cancer cases in the past decades (Jolibois, Guerbet, 2006).

Hospital wastewater can also contribute negatively to the emergence and spread of pathogens multi-resistant to antibiotics (de Souza et al., 2009). Water is not only a means for the dissemination of organisms resistant to antibiotics among the populations of humans and animals, but also the way for the genes for resistance to natural bacterial ecosystems. In such ecosystems, the non-pathogenic bacteria serve as a reservoir of genes for resistance (Baqueiro et al., 2008). The development and dissemination of antibiotic-resistant bacteria were classified by the World Health Organization (WHO) as one of the three biggest threats to human health in the 21st century. As a result of the antibiotics consumption, the normal human bacterial microflora may be altered and extended by bacteria resistant to antibiotics. Humans can be regarded as a source of antibiotics and genes for resistance that enter the environment through sewage systems. The most effective and direct way of reducing the source and dissemination of genes for resistance is probably a sensible use of antibiotics in health care and agriculture (Zhang et al., 2009).

The ecotoxicity of wastewater from medical facilities

Wastewater from medical facilities is a complex mixture of many compounds that may have synergistic, antagonistic or additive effects in organisms (Magdaleno et al., 2014). For the evaluation of the influence of a wide range of pollutants contained in the effluents from medical facilities on the aquatic ecosystems, it is necessary to determine their ecotoxicity (Orias, Perrodin, 2013). There are only a few studies focused directly on the ecotoxicity of wastewater from medical facilities (e.g. Emmmanuel et al., 2005; Tsakona et al., 2007; Boillot et al., 2008; Berto et al., 2009; Zgorska et al., 2011; Magdaleno et al., 2014).

Emmanuel et al. (2005) used ecotoxicological tests with *Pseudokirchneriella subcapitata*, *Daphnia*

magna, and *Vibrio fischeri* to evaluate ecotoxicity of wastewater discharges from the department of infectious and tropical diseases of a hospital in southeastern France. The results of the ecotoxicological tests with *Vibrio fischeri* differed depending on the length of exposure. There were significant differences in the established values of 5 min EC₅₀ compared to 15 min EC₅₀ and 30 min EC₅₀. In 2001, all values of 5 min EC₅₀ were higher than 50 ml l⁻¹ and the hospital wastewater was considered to be non-toxic to *Vibrio fischeri*. In 2002, the lowest determined value of 5 min EC₅₀ was 40 ml l⁻¹. The lowest determined value of 15 min EC₅₀ was 23.8 ml l⁻¹ and 21.7 ml l⁻¹ in the case of 30 min EC₅₀. All samples of hospital wastewater were considered to be toxic to *Daphnia magna*, the lowest determined value of 48 h EC₅₀ was 1.9 ml l⁻¹. The determined values of 72 h IC₅₀ for *Pseudokirchneriella subcapitata* were in the range from 1.8 to 11.1 ml l⁻¹.

Tsakona et al. (2007) monitored the ecotoxicity of samples of hospital wastewater collected both at the outlet from the tank used for chemical neutralization of wastewater from laboratories and at the outlet of the hospital sewage system before its discharge into municipal sewage network. *Vibrio fischeri* was used as the tested organism. The toxicity of wastewater produced by the laboratories at the outlet from the neutralization unit was higher (determined values of 15 min EC₅₀ in the range from 0.396 to 2.036%) than the toxicity of wastewater entering the municipal sewage network (determined values of 15 min EC₅₀ 1.683–6.777%). It is possible to conclude that the laboratories contribute significantly to the toxicity of wastewater.

Boillot et al. (2008) evaluated the ecotoxicity of hospital wastewater samples collected in five intervals during a single day and the ecotoxicity of a mixed 24-hour sample. Ecotoxicity was assessed using the tested organisms *Daphnia magna*, *Pseudokirchneriella subcapitata*, and *Vibrio fischeri*. The biotest battery used for the assessment of ecotoxicity of the mixed 24-hour sample was supplemented by a chronic test with *Ceriodaphnia dubia* (growth and reproduction inhibition test) and a test with *Lemna minor*.

Boillot et al. (2008) stated that the highest ecotoxicity was measured in the samples taken between 9 a.m. and 1 p.m. and the lowest ecotoxicity was measured between 11 p.m. and 5 a.m. The ecotoxicity of wastewater samples decreased in the following order: samples taken between 9 a.m. and 1 p.m. > samples taken between 1 p.m. and 5 p.m. > samples taken between 5 p.m. and 11 p.m. > samples taken between 11 p.m. and 5 a.m. For most of the tested wastewater samples, the values of EC₂₀ were lower than 20%, based on the results of the ecotoxicological tests with *Daphnia magna*, *Pseudokirchneriella subcapitata*, and *Vibrio fischeri*. In the case of the sample taken between 9 a.m. and 1 p.m., the values of EC₂₀ for *Pseudokirchneriella subcapitata* and *Daphnia magna*

were 3.9 and 4.9%, respectively, and the wastewater was considered to be very toxic to the tested organisms. In the chronic test of the mixed sample with *Ceriodaphnia dubia* the value of EC_{20} was 3.1% (in reproductive test) and 24.4% (in growth inhibition test). *Lemna minor* was not sensitive to the tested wastewater and a stimulated growth was observed.

Berto et al. (2009) performed tests of the ecotoxicity of hospital wastewater on algae (*Desmodesmus subspicatus*) and daphnids (*Daphnia magna*). The wastewater was tested at the input and output of the wastewater treatment plant. While no algal growth inhibition was observed in the samples of treated wastewater for any of the tested concentrations, the untreated wastewater was proved to have toxic effects on algal growth depending on the dilution. At the lowest concentrations of untreated wastewater, the sample stimulated the algal growth. A 16% solution of untreated wastewater was the first to show the inhibitory effect (LOEC – Lowest Observed Effect Concentration = 16%) and the effect grew with the increasing concentration of untreated wastewater in the test sample. The untreated wastewater was more toxic (LOEC = 4%) for daphnids than the treated water (LOEC > 100%). As tested organisms, daphnids were more sensitive for the evaluation of wastewater ecotoxicity in this study than algae.

Zgorzka et al. (2011) evaluated the ecotoxicity of hospital wastewater using the following tested organisms: *Pseudokirchneriella subcapitata*, *Daphnia magna*, *Thamnocephalus platyurus*, *Artemisia salina*, and *Vibrio fischeri*. The selected tested organisms represent three trophic levels of the food chain. The tested wastewater samples were collected before treatment in the hospital wastewater treatment plant. Wastewater samples were filtered prior to the ecotoxicological tests. The highest toxic effect was observed in the tests with *Pseudokirchneriella subcapitata* (72 h IC_{50} = 18.77%). The values of EC_{50} based on the results of the biotests with *Daphnia magna* (48 h EC_{50} = 20.76%) and with *Thamnocephalus platyurus* (24 h EC_{50} = 22.62%) were similar to the value of IC_{50} with algae. The lowest ecotoxic effect was observed in *Artemia salina* (24 h EC_{50} = 59.87%) and *Vibrio fischeri* (EC_{50} = 46.17%).

Magdaleno et al. (2014) evaluated the ecotoxicity of wastewater from a public hospital in Buenos Aires. The hospital wastewater is discharged directly into the urban sewage network and is treated with urban wastewater in a wastewater treatment plant. The treated wastewater is discharged into the main source of drinking water for 10 million inhabitants and, therefore, the ecotoxicity of the wastewater on the output of the wastewater treatment plant was evaluated. The tested organism was *Pseudokirchneriella subcapitata*. 55% of the hospital wastewater samples were toxic for algae (algal growth inhibition in the range of 23.9 to 54.8%). In the remaining samples, the stimulating effect of

wastewater on algal growth was observed. Total phosphorus and nitrogen content and organic substances present in high concentrations in the effluents from medical facilities serve as a nutrient for the algae and can act as growth factors (Gautam et al., 2007). On the other hand, compounds such as pharmaceuticals and disinfectants are toxic for algae and may cause growth inhibition. The ecotoxic effect on algae has also been observed in samples collected at the output of the municipal wastewater treatment plant.

Machado et al. (2014) studied the ecotoxicity of wastewater produced by haemodialysis. This wastewater has high conductivity and salinity and exceeds the limits for effluents in Brazil in several other parameters (BOD, COD, concentration of nitrites, etc.) as well. The value of EC_{50} determined in acute tests with *Daphnia magna* was 86.91% ($\pm 0.39\%$). The value of EC_{50} determined in the tests with *Euglena gracilis* was 76.9%. In chronic tests with *Daphnia magna* the values were 72.97% for NOEC (No Observed Effect Concentration) and 94.66% for LOEC (fecundity being the monitored parameter).

Kern et al. (2015) evaluated the ecotoxicity of wastewater from a hospital laundry discharged directly into the municipal sewage network. The laundry contributes to approximately 33% of the quantity of hospital wastewater. The wastewater from the laundry has a different composition than the wastewater from the hospital wards. It shows a high concentration of body fluids (blood, faeces, vomit, etc.), high microbial load, and the potential presence of viruses, pharmaceuticals, detergents, and other cleaning agents and disinfectants. An acute toxic effect of the wastewater from the hospital laundry on *Daphnia magna* (EC_{50} 2.01%) and *Danio rerio* (LC_{50} 29.25%) was observed. Sublethal effects of the wastewater were observed in tests with *Lactuca sativa* (IC_{25} 12.50%) and *Allium cepa* (IC_{25} 51.25%).

Determined ecotoxicity values of wastewater from different medical facilities significantly varied (with EC_{50} ranging from a few to nearly 100 per cent). This variability is caused by the activities in medical facilities, by the season, geographical location, and by the number of patients (Orias, Perrodin, 2013). Toxicity of hospital wastewater for the individual tested organisms also varies significantly (toxicity of wastewater from one medical facility may be up to twenty times higher for some organisms than for the others). Unfiltered wastewater from medical facilities shows higher ecotoxicity than filtered wastewater (Boillot et al., 2008; Orias, Perrodin, 2013).

To gain more knowledge on ecotoxicity of wastewater from medical facilities, it is necessary to continue in chemical and ecotoxicological analyses in other hospitals so that it would be possible to determine the connection between the nature of a hospital and the ecotoxicity of its wastewater (Orias, Perrodin, 2013).

CONCLUSION

Given the growing consumption of pharmaceuticals both in hospitals and in households, it will be necessary to pay attention to both the wastewater from medical facilities and the municipal wastewater and pursue the development of wastewater treatment with regard to the maximum achievable efficiency in the removal of micropollutants and the costs of treatment of large volumes of wastewater.

To assess the environmental and health risks posed by wastewater from medical facilities, further evaluation of the wastewater toxicity and focus on chronic toxicity are necessary. Due to the large variability in the composition of wastewater from medical facilities repeated sampling will be needed to evaluate the long-term ecotoxicity or genotoxicity for organisms at all trophic levels. To obtain relevant results exploitable for developing the standards for the regulation of dangerous substances contained in wastewaters, studies carried out with one or two tested organisms on a small number of samples, as has often been the case, should be avoided. There is a need to develop a single battery of toxicity evaluation tests and provide a single methodology for the individual tests so it would be easier to compare the results of various published studies.

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Corresponding Author:

Ing. Anna C i d l i n o v á, Czech University of Life Sciences Prague, Faculty of Environmental Sciences, Kamýcká 129, 165 00 Prague 6-Suchbát, Czech Republic, phone: +420 605 746 385, e-mail: anna.cidlinova@szu.cz
