Retraction Notice

Title of retracted article: **Endotoxin Occurrence in Raw and Reclaimed Wastewater**
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Journal: **Journal of Water Resource and Protection** (JWARP)
Year: 2014
Volume: 6
Number: 7
Pages (from - to): 688 - 695
DOI (to PDF): http://dx.doi.org/10.4236/jwarp.2014.67066
Paper ID at SCIRP: 9402165
Article page: http://www.scirp.org/Journal/PaperInformation.aspx?PaperID=46226

Retraction date: 14-11-2016

Retraction initiative (multiple responses allowed; mark with **X**):

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 ○ Institution:
 ○ Reader:
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Date initiative is launched: 14-11-2016

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This article has been retracted to straighten the academic record. In making this decision the Editorial Board follows COPE's Retraction Guidelines. Aim is to promote the circulation of scientific research by offering an ideal research publication platform with due consideration of internationally accepted standards on publication ethics. The Editorial Board would like to extend its sincere apologies for any inconvenience this retraction may have caused.

Editor guiding this retraction: Professor Jian Shen (EiC of JWARP)

Journal of Water Resource and Protection, 2014, 6, 688-695
Published Online May 2014 in SciRes. http://www.scirp.org/journal/jwarp
http://dx.doi.org/10.4236/jwarp.2014.67066

Scientific Research

Endotoxin Occurrence in Raw and Reclaimed Wastewater

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Received 9 April 2014; revised 1 May 2014; accepted 16 May 2014

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Abstract

The occurrence of endotoxins in the samples from conventional full-scale activated sludge operated wastewater treatment plants and laboratory scale batch tests were reviewed. High values up to more than 1000 EU·mL^{-1} in secondary effluent were reported and these might present a significant threat to the environment and even potential consumers if potable reuse is considered. The use of membrane biological reactor (MBR) as substitute to conventional activated sludge based treatment was reported to be a suitable alternative since it allows a significant reduction in the final effluent with values of about 300 EU·mL^{-1}. Different post-treatment alternatives were also applied to the secondary effluent of the full-scale plant and/or permeate of the pilot scale MBR units. These are exemplified by tertiary membrane filtration such as reverse osmosis RO and nano-filtration (NF), coagulation-flocculation (CF), adsorption and filtration using sand columns (SC), ozonation and UV treatment and oxidation. Results indicate that CF and RO and NF are the best options to minimize the presence of endotoxins in the final effluent (>90% and up to 65%, respectively). The use of SF was not so interesting since a wide range of removal efficiencies were obtained (44% - 76%) even after a very prolonged contact time (1 year). The efficiency of removal is not stable too in the case of SF. Finally, ozonation appears not to be adequate due to the low removal efficiencies achieved (40% maximum) as well as the potential generation of more endotoxic material during the oxidation process, especially at contact times below 30 minutes.

Keywords

LPS Endotoxin, Wastewater, Conventional Treatment, Advanced Treatment

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How to cite this paper: Mokhtar, G. and Naoyuki, F. (2014) Endotoxin Occurrence in Raw and Reclaimed Wastewater. *Journal of Water Resource and Protection*, **6**, 688-695. http://dx.doi.org/10.4236/jwarp.2014.67066

1. Introduction

Several research works have been reported in the last few decades on the potential risks associated to the operation of Wastewater Treatment Plants (WWTPs) due to the occurrence of a large variety of biological and chemical substances. Special attention has been paid to pathogens present in raw wastewater and reclaimed wastewaters, since these streams have been recognized as an important vehicle for transmission of several viral, fungal and bacterial diseases. In addition, there are also potentially harmful substances, which can be generated during biological treatment processes such as transformation by-products and Soluble Microbial Products (SMPs) generated after metabolic reactions and cell lysis. The SMPs are exemplified by lipo-polysccharide endotoxins, known as LPS endotoxin. While source control can be a useful strategy for the minimization of the entrance of some pollutants in WWTPs, LPS endotoxin will be inevitably present in the final effluents due to their generation along the biological treatment processes and low biodegradability [1]. Endotoxins and, more generally, the exposure to bio-aerosols containing endotoxins, have been considered as a key occupational health risk in wastewater treatment plants and their surrounding environment. Major commonly known risks are related to respiratory and gastrointestinal problems. In this sense, Daneshzadeh-Tabrizi *et al.* [2] indicated that endotoxins are capable of causing an inflammatory reaction at the level of the lung-blood barrier. Since it has been reported several adverse health effects for endotoxin and this organic micro-pollutant can augment the toxic agents, studies to assess endotoxin concentrations and their occurrence in raw and treated wastewater and efficiency of operating water treatment plants to remove them were carried out. Researches exemplified by the works of Uhrbrand *et al.*, [3], Smit *et al.* [4] and Michel Olivier [5] found a relation between bio-aerosol constituents and gastrointestinal diseases such as diarrhea and respiratory disease such as asthma, concluding that microbial exposures such as endotoxins seem to play a causal role. Endotoxin presence in injections and pharmaceuticals are known to cause blood coagulation, thrombosis, and acute disseminated intravascular coagulation, which in turn depletes platelets and various clotting factors, resulting in internal haemorrhaging and lungs, kidneys and liver failures [6]. Information on endotoxin ingestion and inhalation was also reported. However, Selwyn A. Broitman *et al.* [7] reported that endotoxin ingestion by rats might contribute to the development of liver fibrosis and cirrhosis. Investigation on oral exposure to endotoxic LPS has yielded different research papers that attempted to describe LPS inhalation by workers in cotton fields and wastewater treatment plants [5] [8] [9]. More recently, Guizani *et al.* [10] reported that cell exposure to endotoxin induced significant heat shock protein HSP 47 release. Thus endotoxin is considered as emergent contaminant and a new concern for workers in the wastewater industry and an additional challenge for the design and operation of these installations.

Endotoxins are portions of the outer membrane of gram-negative bacteria and some cyanobacteria [11]. Although in many cases this term is used to indicate any cell-associated bacterial toxin, in the field of bacteriology this word is used to refer to the lipopolysaccharide (LPS) complex present in the outer cell wall of that type of bacteria. If fact, the term LPS is commonly used interchangeably with endotoxin since it is considered that LPS is the main cause of endotoxicity [12]. Different works have indicated that LPS endotoxins are toxic to mammals regardless of their bacterial source being this toxicity detected in reclaimed water and effluents from biological reactors [10] [13]. Most studies dealing with endotoxins in wastewater treatment plants are focused on their presence in air streams (bio-aerosols) since the few existing regulatory standards are focused on this phase, such as the recent EU document which indicates that no adverse health effects are expected after chronic occupational exposure at 90 EU endotoxin units (EU) per cubic meter in air [14]. However, the problem is situated not only in the endotoxins present in the bio-aerosols released from the different operations inside a WWTPs, but also in the proper liquid streams, which contain the major fraction of these compounds. In this way Guizani *et al.* [12] stated that nowadays one of the principal emergent issues associated with indirect potable reuse is LPS endotoxins resulting from the SMPs that are abundant in reclaimed wastewater, due to their presence in domestic wastewater and effluents from biological reactors in WWTPs. Effluents of conventional WWTPs have been reported to contain high concentrations, up to 3200 endotoxin units (EU) per milliliter [1], around 320 $ng \cdot L^{-1}$, which is considered as a threat to the environment and even to human consumption, especially if water reuse is considered. Endotoxins have also been detected in different environmental water compartments, such as 86 rivers; reservoirs etc. [15], with concentrations that commonly range much lower values, around 1 - 10 $EU \cdot mL^{-1}$. However, occasional events occurring in nature such as cyanobacteria blooms have been related to the cause of the maximum levels reported, up to 30,000 - 40,000 $EU \cdot mL^{-1}$ [16], which can affect severely the process of drinking water plants. Furthermore, rivers receiving reclaimed wastewater experience high endotoxin values [17]. Although the release of these micro-pollutants is inevitable if biological units are present in the process, it is quite important to understand the occurrence and fate of endotoxins along post-treatment of effluents from conventional WWTPs as well as in wastewater reclamation and reuse treatment processes. Therefore, the objective of this work is to review the occurrence of endotoxins in the effluents of a full-scale conventional activated sludge operated WWTP (CAS) in comparison with a more advanced alternative technique such a membrane biological reactor (MBR). In addition, different post-treatment technologies (membrane tertiary filtration RO/NO, coagulation-flocculation, soil columns adsorption, ozonation and chlorination) are evaluated in order to minimize the content of endotoxins in the final effluent of the conventional WWTPs taking into account its further use for water reclamation.

2. Secondary Treatment

2.1. Endotoxins in Full-Scale WWTPs

There is only very limited information available on raw and reclaimed wastewater endotoxin concentrations. Previous works include the assessment of endotoxin activity in the influent and effluent of full-scale WWTP based on the use of a biological reactor designed only for the removal of suspended solids and organic matter. Average samples were collected from the influent and final effluent (supernatant of secondary settler) taking into consideration the seasonal variation. Data from separate investigations indicate that endotoxin levels in raw and reclaimed wastewater range from 50 to 9800 EU/mL. highest values were observed in plants receiving return sludge from sludge treatment facilities [18]. These levels would certainly be of concern if they were found in water intended for potable reuse. Data from lab batch tests confirm above findings with endotoxin levels of more than 5000 EU·mL^{-1} in return sludge [1].

The overall range of values obtained was quite wide, from 65 up to 843 EU·mL^{-1}, with seasonal averages of 310, 354 and 182 EU·mL^{-1}, for winter, spring and summer respectively. From these data it is not possible to establish a seasonal dependence more than the largest variations observed in spring (with the lowest and highest values) and the lowest average obtained in summer. Although data available about endotoxin occurring in the liquid phase are scarce, some previous reports focused on the determination of endotoxins present in air samples in STPs indicate higher concentrations during summer or no significant differences between seasons [19]. Apart from temperature, other factors, such as the origin of wastewaters, type of technology, mode of operation, etc., should be taken into account, in order to determine their influence on endotoxin release. In this sense, the use of surface aerators (as occurs in the analyzed full-scale STP) might promote a higher release of endotoxins due to their inherent higher stress applied to the biomass agglomerates.

2.2. Membrane Biological Reactor

According to Guizani *et al.* [10], a pilot-scale MBR equipped with a polyvinylidene-fluoride (PVDF) Toray submerged flat sheet membrane module as well as a PVDF polymer Hollow-fiber MF membranes (Mitsubishi Rayon Engineering, Tokyo, Japan) was installed in the WWTP in order to operate with the same influent (sewage after primary treatment) that the full-scale biological reactor receives. The main characteristics of this membrane are an average pore size of 0.1 μm and a nominal surface area of 6.8 m^2. This pilot plant was operated at a hydraulic retention time of 12 h and at different extended sludge retention times to increase biomass concentration and to favor sludge adaptation.

The pilot-scale MBR was operated along one year treating the same stream as the full-scale CAS unit. **Figure 1** shows the concentration of endotoxins present in the final effluent of the MBR system (permeate) together with the values obtained for the CAS unit. It can be easily seen that the concentrations of endotoxins in the permeate are substantially lower than those determined in the full-scale STP, with values ranging 650 - 1170 EU·mL^{-1}, which imply that the MBR unit is able to reduce the amount of endotoxins from 58% up to 90% in comparison with the mentioned conventional full-scale bioreactor.

In order to determine if this reduction is only carried out by physical meanings (membrane size exclusion), the content of endotoxins was determined in the MBR both in the mixed liquor and in the permeate. The results showed that average values of 860 and 30 EU·mL^{-1} were contained in both compartments, respectively, thus indicating that the physical effect caused by the membrane is the key factor (66% reduction). In addition, taking into account that the level of endotoxins in the effluent of the full-scale STP during the days corresponding to these experiments was 2802 EU·mL^{-1}, it seems that apart the effect of the membrane, the MBR reactor is able to

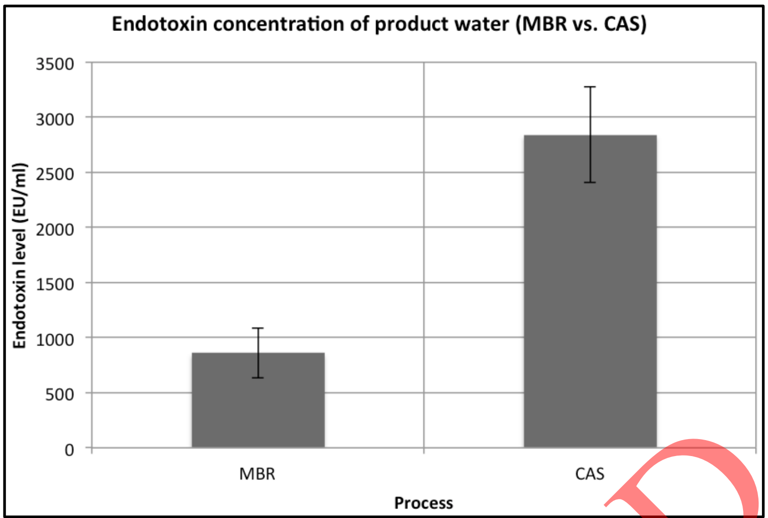

Figure 1. Endotoxin concentration in MBR permeate and CAS effluent.

maintain a lesser amount of endotoxins in the liquid media. Although this observation should be subjected to further confirmation, the different way of operation between both systems (solids retention time) and, especially, the different aeration systems (surface aerators in the full-scale plant versus diffuse aeration in the MBR) might have an influence to explain this difference.

It should be noticed that the endotoxicity of the permeate increases as biofilm is formed on the membrane surface which causes a drop in membrane flux.

3. Advanced Treatment Strategies to Control Endotoxicity

Different advanced treatment systems were applied to the effluents of the secondary settler of the full-scale WWTP such as membrane filtration, coagulation-flocculation, soil column filtration and adsorption as well as ozonation and oxidation, with the aim to reduce the presence of endotoxins in the final effluent of the plant.

3.1. Membrane Technology Treatment Using MF, NF and RO

Although secondary membrane bio reactors (MBR) systems have been reported to produce the best results in terms of producing a high quality final effluent feasible for reuse purposes [20], the use of Tertiary Membrane Filtration (TMF) systems has been considered as a competitive alternative to upgrade existing activated sludge processes, especially if land cost is not crucial, which is the situation in many small and medium-sized municipalities. In fact, TMF systems are currently replacing many sand filters used for tertiary treatment, since the final effluent characteristics are better [21].

In terms of endotoxin reduction, nano-filtration and reverse osmosis were used as post-treatment in the configuration known as TMF following micro filtration to test the removal of endotoxins. A micro flat sheet membrane filter from Toray (Japan) with a pore size of 0.1 μm and a nominal surface area of 6.8 m^2 as well as a hollow-fiber membrane filter from Mitsubishi Rayon engineering (Japan) with a pore size of 0.4 μm were used to test endotoxin removal Guizani *et al.* [10]. The permeate of the flat sheet membrane was treated, in a parallel setting, using a two-inch spiral wound polyamide NF membrane (LES90) and an RO membrane (ES10) from Nitto Denko, Japan. Salt rejection rate is 90% to 99.5% respectively and permeate flux is fixed to 0.46 $m^3 \cdot d^{-1}$. Basically, the objective to run these experiments was to determine the effect of long time operation on endotoxin removal. It has been revealed that the biofilm formed on membrane surfaces contribute to the release of some low molecular weight endotoxin material that passes through the membranes. Larger endotoxin molecules were also produced and at a longer sludge retention time, these were biodegraded to a smaller molecule that passes through the membrane. These findings, explain the high endotoxicity observed in permeates as times progresses [1].

Endotoxin concentration in the NF and RO permeate has been found to be higher than that recorded in tap water and groundwater. Causes of increase in endotoxin toxicity in the NF and RO permeates is not yet understood. Although the absence of endotoxin in drinking water standards, reports that for a successful potable reuse two ways can be approached [22]. First, dilution of NF and RO permeates with drinking water to reach a level close to that frequently detected in potable waters. Second, is to proceed for further treatments, such as long-term storage and oxidation of endotoxins present in water.

3.2. Coagulation-Flocculation

According to Guizani *et al.* [12], most of the dissolved organic matter showing endotoxicity in effluents from WWTPs is hydrophobic and thus, susceptible to interact and be removed with conventional coagulants. Thus, coagulation-flocculation (CF) assays were carried out in a Jar-Test device, using 500 mL of liquid samples collected from the effluent of the secondary settling tank. The influence of aluminium, a common additive in water treatment as coagulants, was studied testing a concentration of 10 mg·L^{-1}. The assays were conducted at ambient temperature, *i.e.* 15˚C - 20˚C. The test included an initial 1 min period of rapid stirring (110 rpm), after the addition of the coagulant, followed by 30 min of slow mixing (25 rpm) for emulsion breaking and flock formation, and finally a 30 min period for settling without mixing, for flock separation. Since the objective of the work was to enhance endotoxins removal prior to the discharge of the final effluent, all the experiments were carried out at the pH range of 4.5 - 7.7. Samples for LAL determination were taken at beginning and the end of this experiment, being all assays performed in duplicate.

Two sets of assays were carried out with initial endotoxin concentrations in the range 900 - 1150 EU·mL^{-1} in order to determine the optimal dosage and pH. The authors report that the coagulants was able to remove significant amount of the endotoxins present in the secondary effluent, with optimum removal efficiencies 30% obtained with a pH ranging from 6.0 to 7.4 [22].

It may be suggested that studies should investigate the effect of using different type of coagulants on endotoxin removal such as ferric chloride, aluminiumsulphate and aluminiumpolychloride (PAX). An estimation of the optimum conditions for endotoxin removal and the amount of coagulant required would be a good alternative for a cost efficient endotoxin removal.

3.3. Soil Adsorption and Filtration

Soil-aquifer treatment (SAT), was investigated for its capacity to treat endotoxins [23]. Effluent for full-scale activated sludge wastewater treatment plant was run through soil columns under gravity flow conditions. Various soil filter materials (fine sand, medium sand, coarse sand and very coarse sand) were used. Endotoxin transformation exhibited different profiles, depending on the time and soil type. Reduction in endotoxin concentration averaged 64.3% and was as high as 86.7% across the very coarse sand and fine sand. Tests were performed to evaluate the transformation of organic matter showing endotoxicity and to determine the mechanisms responsible for changes in the structural and size properties of dissolved organic matter (OM) during SAT. Dissolved OM was fractionated using Sep-Pack C18 Cartridges into hydrophobic and hydrophilic fractions. Dialysis tubes with different molecular weight cut-offs were used to perform size fractions of OM showing endotoxicity. Evaluation of the transformation of organic matter showing endotoxicity during SAT indicated that both hydrophobic and large molecules were reduced. Moreover, experimental findings showed that adsorption test data fit to the Freundlich isotherm and were affected by the particle grain size with higher adsorption capacity for fine and medium sand. Long-term operation of SAT endotoxin is under investigations. Preliminary results reveal that endotoxin removals not stable.

4. Advanced Treatment Strategies to Control Endotoxicity

It is worth reporting about other advanced treatment alternatives that were tested for endotoxin removal from water. The below alternatives were related to endotoxin in drinking water but not in treated wastewater.

4.1. Ozonation

A. Rezaee *et al.* carried out a study on endotoxin inactivation in surface water, using ozonation [24]. The efficiency of ozone for endotoxin inactivation increased with increasing exposure time and ozone concentration, but it was independent of preliminary endotoxin concentrations and pH variation. Ninety minutes exposure to 1

L/min ozone was adequate to inactivate 200 EU/mL of endotoxin. During the experiment, it was observed that the conditions existingduring exposure of the endotoxin to the ozone affected the rate of inactivation. These conditions included excess foaming and bubble size, which related to the contact time of the ozone to endotoxin. By controlling these variables, however, reproducible end points were achieved. These results suggest that ozonation process will be able to inactive endotoxin from water.

Guizani *et al.* are carrying on ozonation assays in a pilot-scale installation to test endotoxin removal from secondary effluent of activated sludge process. Their findings were not yet published.

Because variation of pH does not affect the rate of endotoxin inactivation it was suggested that ozonation process could be used in neutral point of pH that this phenomena is very appropriate from the point of view of drinking water treatment.

4.2. UV Treatment and Oxidation

Anderson et al studied endotoxin inactivation using UV lamp [25]. However no information is available in about operational conditions. His results report that an inactivation rate of 0.55 (Eu/mL)/(MJ/cm). It should be noticed that his work dealt with endotoxin release by ocyanobacteria blooms in water reservoir. Guizani, M. has also performed some preliminary studies on endotoxin removal using UV treatment and oxidation. The samples were exposed to sunlight for few hours to few days. A rate of 1% removal was observed for 8 hours exposure to sunlight (Unpublished). In some cases endotoxin concentration has increased. Bacterial blooms in favorable conditions might cause this increase in endotoxicity.

4.3. Chlorination

Although, several studies reported that chlorination is effective for inactivation of water endotoxin [16]. But, it was showed that in presence of 2 and 100 mg/L free chlorine residual the inactivation rate is 1.3 - 1.4 Eu/mL and this rate is independent of starting concentration, so free chlorine would be relatively ineffective in endotoxin control and removal. However, chlorine based inactivation of endotoxin in presence of ozone is very higher than rates that was reported [25]. This higher inactivation rate can be related to oxidation power of ozone that is higher than chlorine.

5. Discussion

It is important to note that high endotoxin concentration might occur in high concentration in reclaimed wastewater as a result of high release during biological reaction and low biodegradability which may confound observations in full-scale systems [1]. Advanced treatment alternatives are therefore necessary to reduce these contaminants to lower levels. An because there is no standards yet for endotoxin exposure through ingestion, acceptable levels of exposure should be in the range of endotoxin levels found in ground and tap water, roughly 50 $EU \cdot mL^{-1}$ [15]. Advanced treatments, reported in the literature, could achieve a significant reduction of endotoxin concentration. However, final values are higher than that of ground and tap water [22]. Therefore, techniques for a safe reuse of reclaimed wastewater should be considered and these may include, but not to limit to, dilution with potable water.

Furthermore, studies should be directed to determine safe endotoxin levels in drinking water since no guideline values for endotoxin concentration exist.

6. Conclusion

The occurrence of significant concentrations of endotoxins (up to 843 $EU \cdot mL^{-1}$) has been determined in the effluents of the secondary settler of a conventional full-scale activated sludge plant along a three-year monitoring campaign, considerably higher than those present in the effluents of more innovative systems such as a MBR (always lower than 100 $EU \cdot mL^{-1}$). Therefore, conventional STPs can be considered as an important entrance of this type of micro-pollutants into the environment. In those cases where an post-treatment stage is considered to upgrade CAS systems in order to achieve higher efficiencies in meeting effluent standards (turbidity, particles, microorganisms and microbial pathogens), its potential effect on endotoxin removal should be also taken into account. From the results obtained, it is clear that the use of coagulants as well as TMF units is the best options to minimize the presence of these substances in the final effluent (>90% and up to 72%, respectively). The results obtained with activated carbon were not so clear, with removal efficiencies around 40% - 72% after a prolonged contact time. Finally, the results obtained with ozone were in a lower range (32% - 40%), with the additional problem of the complex removal kinetic observed which involves also the generation of new endotoxic matter. As a main conclusion, this work confirms the suitability, in terms of endotoxins removal, of the use of the two main membrane-based wastewater reclamation and reuse treatment methods for non-potable water usage: low pressure membrane tertiary filtration after conventional biological wastewater treatment (CAS-MF), as well as membrane biological reactors. This is a key issue taking into account that effluent wastewater reuse (for both non-potable and potable purposes) has been a subject of increasing importance compared as other alternatives such as desalination, since major advantages regarding cost and sustainable environmental benefits can be achieved.

Acknowledgements

The authors wish to acknowledge the financial and technical support provided by Sapporo Sewer bureau.

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