Biological Treatment of Pharmaceutical Waste Water from the Antibiotic Industry

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Abstract

SBRs (sequencing batch reactors) and MBRs (Aerobic membrane bioreactors) were used to treat the pharmaceutical firm's effluent, which came from an antibiotic (Penicillin) company. Both kinds of reactors were able to treat wastewater when the organic loading rate was low, or 0.22kg-COD m3d1, such that the treated wastage complied with discharge regulations other than for the TDS. However, there were problems with foaming when the loading rate was raised to 2.92kg-COD m3d1, which further contributed to inconsistent performance. In terms of the aromatic chemical degradation, as measured by UVA (UV absorbance), it was found that the SBRs outperformed the MBRs in solid removal. Finally, two different streams were subjected to ozonation, and the results on the strong streams—which correspond to the formulation effluent and include the majority of the bio-refractory compounds—showed promise. Successful ozonation resulted in a reduction in UVA, a decrease in pH, and a rise in the ratio of the strong stream's BOD5: COD (biochemical oxygen demand to chemical oxygen demand). Due to its lack of selectivity for refractory chemicals, it was less effective when applied to effluents that had already received pre-treatment by a bio-filter.
Keywords: Membrane bioreactor, sequencing batch reactor, biological treatment, ozonation, pharmaceutical wastewater.

Introduction:

Pharmaceutical effluent is often known for its very high toxicity levels and the inclusion of refractory chemicals that restrict its biodegradability and, as a result, render it potentially dangerous to the nature and even wastewater treatment facilities if not treated correctly (Gros, 2010).

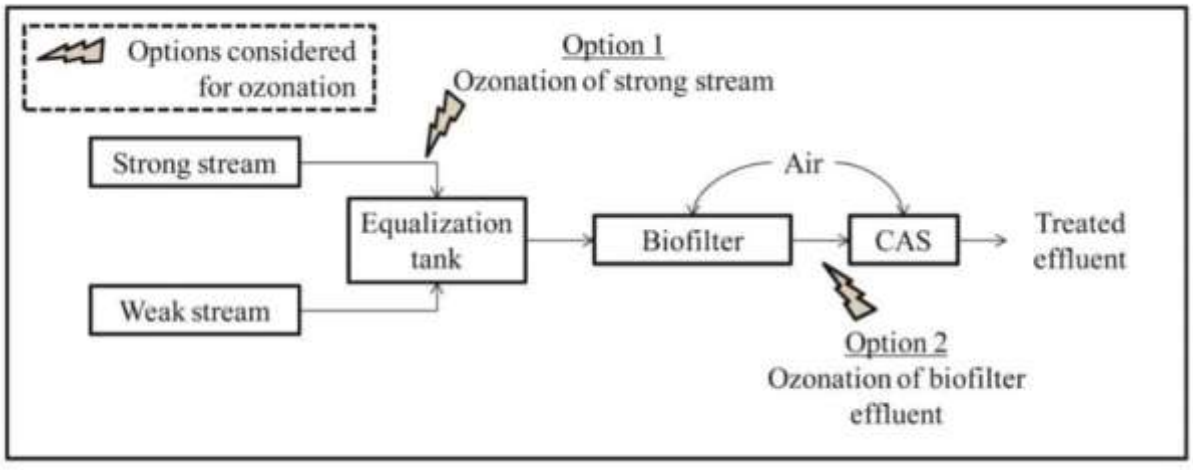
The production of pharmaceutical agents goes through many steps, including the fermentation, extraction, and chemical synthesis of natural molecules into medicinal components. The packaging and formulation of the products come after the preliminary procedures (Oktem et al., 2008).In addition, a report claims that 200 to 30,000kg of waste may be produced for each kilogram of active ingredient generated during the pharmaceutical production process, making the variety of wastes generated during this process significantly greater than the amount of the actual final product (NDRC 2009). The pharmaceutical composition of by-products differs depending on the kind of medicine being produced, the materials utilized in synthesis, and the

particular processes that are followed. They may consist of biological materials such as fermentation wastes, excess extraction solvents left over after isolating and purifying the active compounds from natural sources, any pharmacologically active substances such as chemotherapeutic and anticoagulants agents, and dis-infecting and cleaning agents typically utilized to sterilize equipment.

The concentration of pollutants in the wastewater stream is also influenced by the medicine preparing process. For instance, the reduced effluent flow and low pollutant wastewater stream load formed while cleaning the equipment are two characteristics (weak stream).However, the effluent that is produced during the formulation process is far more severely contaminated and is often referred to as a strong stream. Due to the high concentration of active chemical compounds present, the formulation wastewater has a lower biodegradability, which causes this (Otker & Balcioglu, 2003). Pharmaceutical wastewater, which may have a COD value as high as 80,000mg/L, ultimately includes the pharmaceutical drugs prepared from the different manufacturing lines of pharmaceutical production plants (Kaul &Nandy, 2001).

The many types of medicines create specific problems, and among them, antibiotics have a considerable influence on the environment where they may interfere with the process of treating wastewater and can negatively damage ecosystems (Schroder et al., 1999; Sim,2010). Moreover, certain bio refractory elements that are difficult to decompose may be present in the pharmaceutical wastewater that emerges from the manufacturing of antibiotics (Schroder et al., 1999). Additionally, biological therapy may be an effective option for the treatment when combined with physiochemical processes (Zhou, 2006). Anaerobic treatment may be an appropriate alternative given the high COD concentration of pharmaceutical wastewater, but it is never practical due to the waste water's high TDS (total dissolved solids) concentration, which inhibits the action of methanogenic bacteria (Moletta & Lefebvre, 2006).

In the investigation, wastewater was first gathered from a pharmaceutical plant that produced the antibiotic Penicillin. On-site production of two different wastewater streams included a strong stream, which matched the formulation waste matter and was distinguished by a weak stream, and a very high organic content. The strong-to-weak stream ratio is 1:2 (v/v).The figure below schematizes the present on-site treatment process:



The pharmaceutical company's present wastewater treatment procedure is shown in the figure, along with the ozonation alternatives that were taken into consideration for this research.

In an equalization tank, the two streams were combined where phosphoric acid was added to bring the pH level down to 7 and urea was administered as a source of readily accessible

nitrogen. The combined stream is then subjected to further aerobic treatment using a biofilter and CAS (conventional activated sludge).

The following two alternatives to the aerobic treatment method were taken into consideration in the study: The SBR is also renowned as being a very resilient system ideal for the industrial wastewater treatment collected from the food sectors and dairy sectors. Both the MBR and the SBR are noted for their ability to reliably generate high-quality effluent free of suspended particulates (Torrijos, 2004, Lefebvre, 2005).Additionally, batch studies were used to assess the effectiveness of ozonation in improving the biodegradability of pharmaceutical waste water. Once again, there were two options: ozonation of the strong stream, which had already been introduced to the CAS and included the majority of the bio-refractory effluent.

Method:

Wastewater collection and Preparation-

The pharmaceutical firm first provided the weak and strong stream of the wastewater, which were both collected and held at a temperature of 4ºC in the dark. Weak and strong streams were combined at 1:2 (v/v) ratio before being fed into the bioreactors, creating a mixed stream whose pH was raised to 7 by adding content 0.28g/L of urea and phosphoric acid. This stream was then supplied to the SBR and MBR bioreactors, which will be discussed later. The actual plant's biofilter effluent, which had been utilized for ozonation studies in the batch testing, was also taken, and it was then kept in the dark at 4ºC and used without further changes.

Bioreactor setup-

The SBR and MBR, two distinct biotechnologies, were used in this study. All of the reactors were run in duplicate. The flat sheet polyolefin membranes for the aerobic MBRs (working volume = 7L) had nominal pore sizes of 0.45μm and were coupled to a single module support, which was submerged into each MBR. Each module has an effective membrane area of $0.11m^2$and the clean membrane surface had a contact angle of 72º (Ng & Ng 2010).The 8-minute suction cycle was followed by a 2-minute relaxing period. Additionally, the membrane modules were removed from the reactors weekly and their surfaces are carefully cleaned using a sponge. Since there was no serious fouling, chemical cleaning was not necessary during the whole trial. The 4L working volume aerobic SBRs were run for 24h in cycles that lasted 40 minutes for feeding, 22.3h for the response, 30 minutes for settling, and 30 minutes for withdrawal. All of the reactors were performed at a hydraulic retention time (HRT) of around 7-8 days and an ambient temperature of (25±5ºC). The average SRT (solid retention time) for MBRs and SBRs was found to be 50 days and 20 days, respectively.

Ozonation-

Utilizing an Ozonia Triogen laboratory ozone generator, the ozonation procedure was carried out (Suez environment, France). 5L/min of oxygen from a bottle was used to create ozone. Batch mode was used for this ozonation. A 500ml Drechsel container was used to treat 150ml of the effluent for each batch. By deducting the excess and residual ozone from the actual ozone dosage, or unreacted and residual ozone, the demand for ozone was calculated. The iodometric titration semi-batch technique of Standard approaches (APHA, 2005) was used to determine the ozone exposure, which was calculated to be 5.6g/h under experimental circumstances. The residual ozone in the effluent was detected using the Indigo colorimetric technique, and the surplus ozone exiting the reactor vessel was quantified by trapping it into a gas cleaning bottle consisting potassium iodide (APHA 2005).The samples were collected and examined at

predetermined intervals during ozonation.

Analyses-

Following the AFNOR guidelines, TDS, VSS: "Volatile Suspended Solids", and TSS: "Total Suspended Solids" was defined by centrifugation at 15,000rpm for 15 minutes (1). Following this, the supernatant underwent standard techniques analysis for pH, dissolved COD, and BOD5 (APHA 2005).Additionally, absorbance at 254nm (UVA, and 580nm), which matched yellow-orange, the natural hue of the wastewater, and color were determined. Using a TOC/TN analyzer, the TN (total nitrogen) and TOC (total organic carbon) were measured (Shimadzu, Japan).After filtering using 0.45μm glass fiber filters, the concentrations of nitrate (NO_3-), ammonium (NH4+), nitrite (NO2-), sulphates (SO42-), and phosphate (PO43-) were measured using ion chromatography (Dionex, United States).With bright field illumination, the gram-stained foam bacteria were examined under an X100 oil immersion objective for microscopic inspection.

Results & Discussion-

Wastewater Characterization:

The table below shows the specifics of the characterization of the various streams utilized in this investigation. The basis for this presentation was a weekly analysis during the whole trial period.

	Strong stream	Weak stream	Mixed stream	Biofilter effluent
COD (mg L^{-1})	54,800 ± 964	6,877 ± 321	19,099 ± 3,614	11,985 ± 1,004
BOD_5 (mg L^{-1})	33,975 ± 6,390	5,957 ± 1,585	16,148 ± 1,578	10,919 ± 874
TOC (mg L^{-1})	20,367 ± 84	4,147 ± 209	8,125 ± 1,472	5,605 ± 646
UVA (cm^{-1})	138.9 ± 37.5	4.3 ± 0.5	17.0 ± 2.9	32.6 ± 4.9
Color (cm^{-1})	0.25 ± 0.04	0.25 ± 0.12	0.24 ± 0.08	1.17 ± 0.25
TN (mg L^{-1})	3,923 ± 400	582 ± 39	1,967 ± 158	1,978 ± 102
NH_4^+ (mg L^{-1})	360 ± 59	11 ± 2	N.D.	N.D.
NO_3^- (mg L^{-1})	13 ± 1	5 ± 1	N.D.	N.D.
NO_2^- (mg L^{-1})	10 ± 1	b.d.l.	N.D.	N.D.
pH	11.3 ± 0.4	6.3 ± 0.2	7.3 ± 0.1	8.9 ± 0.1
TDS (mg L^{-1})	66,793 ± 1,362	6,447 ± 640	25,846 ± 1,442	28,772 ± 642
TSS (mg L^{-1})	240 ± 113	153 ± 50	234 ± 55	1,256 ± 294
VSS (mg L^{-1})	107 ± 80	80 ± 56	124 ± 69	928 ± 234
$P\text{-}PO_4^{3-}$ (mg L^{-1})	0.9 ± 0.1	3.7 ± 1.1	640 ± 236	430 ± 89
SO_4^{2-} (mg L^{-1})	670± 127	55 ± 48	N.D.	N.D.

N.D. – not determined; b.d.l. – below detection limit.

The characteristics of pharmaceutical wastewater are shown in the table. The weak and strong streams were combined in the laboratory at 1:2 (v/v) ratio, the pH was raised to 7 using phosphoric acid, as well as 0.28gL^{-1} of urea was added.

The high UVA and COD, low ammonium content but high nitrogen content, and exceptionally low phosphorus concentrations were the characteristics of the strong stream. Additionally, neutralization was necessary before the biological treatment because of the pH of 11.3 of the strong streams. The weak stream, on the other side, had lower pH, UVA, and COD levels, but it also lacked phosphorous and easily accessible nitrogen. The limitations of Nitrogen and Phosphorous were both addressed in the mixed stream by the inclusion of phosphoric acid and urea. Consequently, the C:N:P ratio of the mixed stream averaged 100:20:5, revealing that both Nitrogen as well as Phosphorous were not only adequate but also somewhat excessive. Overall, the mixed stream's pH value was 7.3 and its BOD5: COD ratio was 0.8, making it fully

acceptable for biodegradation. Similar to the mixed stream, the bio-filter effluent had a high COD content that was, on average, 47% higher. However, due to the biomass washout from the bio-filter, its pH was more alkaline and its VSS and TSS levels were greater. The improved total biodegradability is explained by the increased biomass concentration in the bio-filter wastewater.(Ratio of BOD5: COD of 0.9) between the mixed stream and the bio-filter effluent.

Performance of biological treatment -

The aerobic treatment of the industrial wastewaters in the investigation was done upon the mixed stream at two distinct OLR (organic loading rates):a high OLR(2.92 ± 0.44kg $CODm^{-3}d^{-1}$) and a low OLR(0.22 ± 0.03kg $CODm^{-3}d^{-1}$). The findings are shown in the table below. The low value of OLR was achieved by adding diluted effluent to the reactors under each OLR for a three months trial.

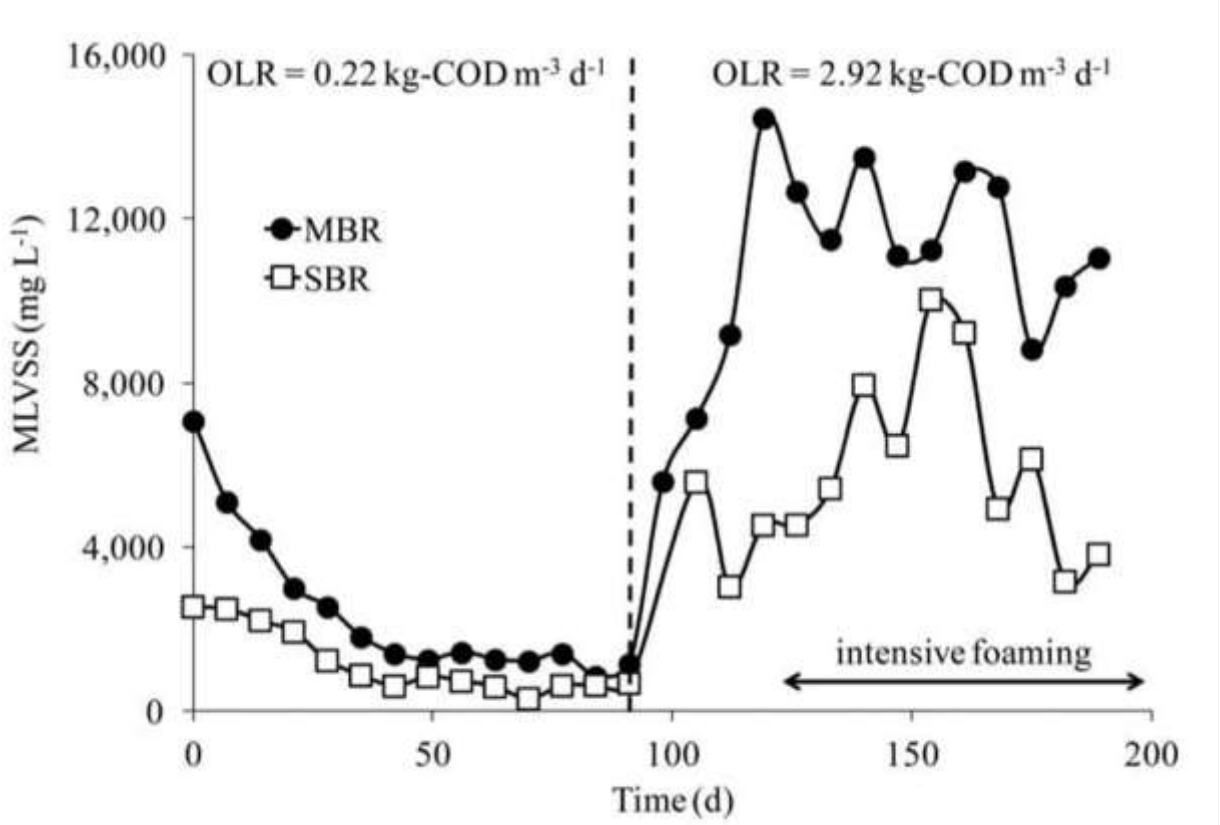
	0.22 kg-COD m $^{-3}$ d $^{-1}$				2.92 kg-COD m $^{-3}$ d $^{-1}$			
	MBR		SBR		MBR		SBR	
OLR	Treated effluent	*RE (%)*	Treated effluent	*RE (%)*	Treated effluent	*RE (%)*	Treated effluent	*RE (%)*
COD (mg L^{-1})	184 ± 35	*89 ± 2*	135 ± 12	*92 ± 1*	3,246 ± 977	*87 ± 3*	3,152 ± 1,419	*82 ± 10*
BOD_5 (mg L^{-1})	3 ± 1	*> 99*	2 ± 1	*> 99*	313 ± 256	*98 ± 2*	933 ± 710	*95 ± 4*
TOC (mg L^{-1})	123 ± 37	*82 ± 5*	61 ± 11	*91 ± 1*	628 ± 392	*86 ± 13*	644 ± 265	*90 ± 6*
TN (mg L^{-1})	362 ± 55	*0*	159 ± 33	*18 ± 16*	1,677 ± 1,522	*0*	687 ± 459	*67 ± 23*
P-PO_4^{3-} (mg L^{-1})	168 ± 76	*0*	75 ± 67	*0*	949 ± 353	*0*	906 ± 331	*0*
TDS (mg L^{-1})	5,460 ± 576	*0*	3,315 ± 78	*0*	38,792 ± 2,036	*0*	35,938 ± 5,410	*0*
TSS (mg L^{-1})	12 ± 8	*95 ± 7*	148 ± 49	*0*	105 ± 43	*55 ± 24*	2,792 ± 1,947	*0*
VSS (mg L^{-1})	3 ± 7	*97 ± 9*	115 ± 65	*0*	57 ± 33	*52 ± 37*	2,097 ± 2,117	*0*
UVA (cm^{-1})	1.2 ± 0.3	*46 ± 12*	0.8 ± 0.1	*60 ± 5*	19.8 ± 3.4	*8 ± 9*	11.1 ± 3.0	*33 ± 17*
Color (cm^{-1})	0.02 ± 0.01	*86 ± 9*	0.01 ± 0.01	*93 ± 7*	0.08 ± 0.04	*36 ± 23*	0.11 ± 0.05	*34 ± 34*

RE = removal efficiency.

The table displays how bioreactors that treat pharmaceutical wastewater perform with loading rate.

The BOD5, COD, and TOC removal efficiencies that were assessed in the diluted fraction were also somewhat greater in the SBRs than MBRs (on average, 99, 92, and >91 percent, correspondingly). At least OLR, the MBRs demonstrated greater VSS and TSS removal. Additionally, both the SBRs ($93\pm7\%$) and MBRs ($86\pm9\%$) had outstanding color removal.The UVA removal was considerably high-level in the SBRs as compared to MBRs (on mean 60% versus 46%), and the enhanced performance may also be attributed to the SBRs' ability to retain sludge almost as effectively as the MBR integrated to enhance the trapping and adsorption of the organic concentration in the sludge during the settling stage (Lafabvre, 2005). The results were consistent with the findings of Ng et al. (1989), who discovered that an SBR, after pre-treatment with Feuton's oxidation, could remove about 98 percent of the COD of wastewater produced by a medicine production plant situated in Turkey (Tekin et al., 2006).Unexpectedly, since they were delivered in excess, the phosphorous and nitrogen removal efficiencies were minimal in both kinds of reactors. All of the metrics (BOD5<400mg/L, COD<600mg/L, and TSS<400mg/L) fulfilled the discharge conditions as per Singapore's rules for discharge in the public drains at low OLR, except for TDS (TDS>3000mg/L).

According to the figure below, the MLVSS (mixed liquor volatile suspended solids) stabilized after 42 days at 600mg/L in the SBRs and 1200mg/L in the MBRs.



The development of MLVSS in the bioreactors used in the experiment is shown in the above figure with the OLR.

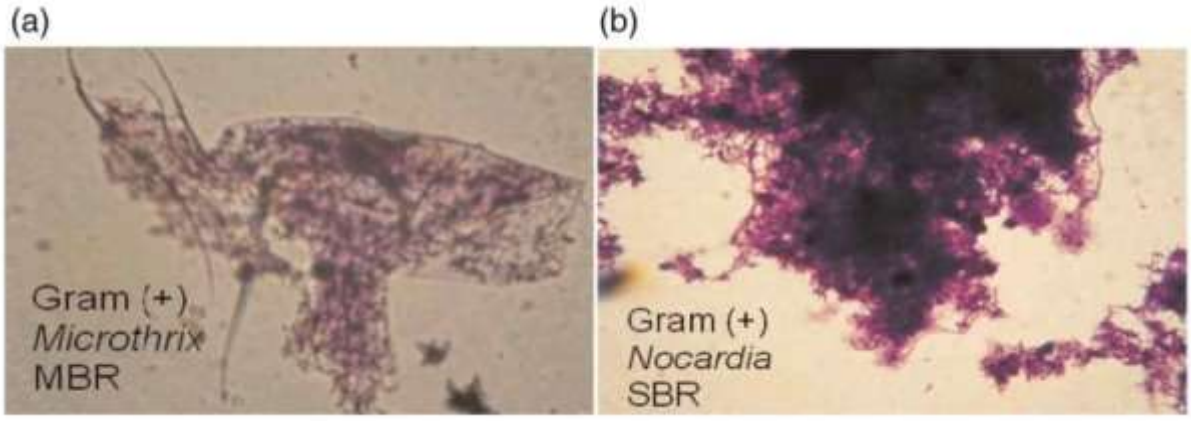
The amount of biomass wasted (derived through the SRT of 50 days and 20 days, correspondingly, for SBRs and MBRs in a period that is represented in g-VSSd^{-1}) and the total biomass accumulated (slope of the figure) were added together, and the result was divided by the amount of BOD that is consumed for the same duration (written in g-BOD5/d).The average biomass output measured between days 91 and 42, which corresponded to steady operation at low OLR, was 0.2 and 0.1g-VSS g-BOD-1 in SBR and MBR, correspondingly. The results are much lower than those seen in conventional biological treatments (~0.4g-VSS g-BOD-1), and the following are some likely causes:

(i) Since the loading rate was so low, endogenous respiration was higher than typical.
(ii) The potential existence of chemicals in wastewater impedes development.

This may be due to the antibiotics in the wastewater from pharmaceutical manufacturing facilities, which still can prevent the development of a variety of microbes (Wollenberg, 2000). The by-products that were generated during the biological therapy are the second potential cause of inhibition. A quick rise in MLVSS was seen at a high OLR value of 2.92kg-COD$m^{-3}d^{-1}$ up to 14,450mg/L in the MBR on average, which was only a little bit higher than the highest value of 10,000mg/L attained in the SBR's (depicted in the figure above).This amount is under the observed growth yield, which is 0.3g-VSS g-BOD-1 and is almost comparable for both SBRs and MBRs. The results are still a little bit lesser than what is theoretically predicted, revealing a possible inhibition from leftover by-products and antibiotics, but they are still much greater than the value that is produced at lower OLR. The high endogenous respiration rate was rather a very strong indication that it was the major cause of the poor biomass development at low OLR.Even while the BOD5, COD, and TOC removal capabilities were up to 98, 87, and 90 percent,

correspondingly, the biomass increase was also followed by a decline in the reactor's performance, and the discharge condition was no longer fulfilled (demonstrated in the second table).

The bioreactors being overloaded due to the high loading rate was the most likely and appropriate cause. In addition, despite using a lot of defoaming agents, all of the reactors were shown to be quite unstable and often foaming was detected. The declines in the MLVSS that were seen in both SBRs and MBRs after 120 days may be explained by the following loss of the biomass that followed the foaming occurrences (demonstrated in the figure above). Microthrix and Nocardia are two bacterial genera that are often linked to foaming in the aeration tank. In the foam samples that were collected from both reactors, both of these microorganisms were recognized under microscopy (demonstrated in the figure below). These bacterial genera are present, and their existence is directly related to the high aeration rates (Tchobanoglous et al. 2004).The hydrophobic cell surfaces of Microthrix and Nocardia both attach to the air bubbles, forming foam. Due to the very high BOD and COD content in the experiment, a high aeration rate was needed to keep the dissolved oxygen content in MBRs and after SBR cycles over 4mg/L at all times. It should be noted that neither biomass settling in SBRs nor membrane filtration in MBRs was ever affected at the high OLR, demonstrating the effectiveness of both techniques for the accumulation of significant amounts of biomass.

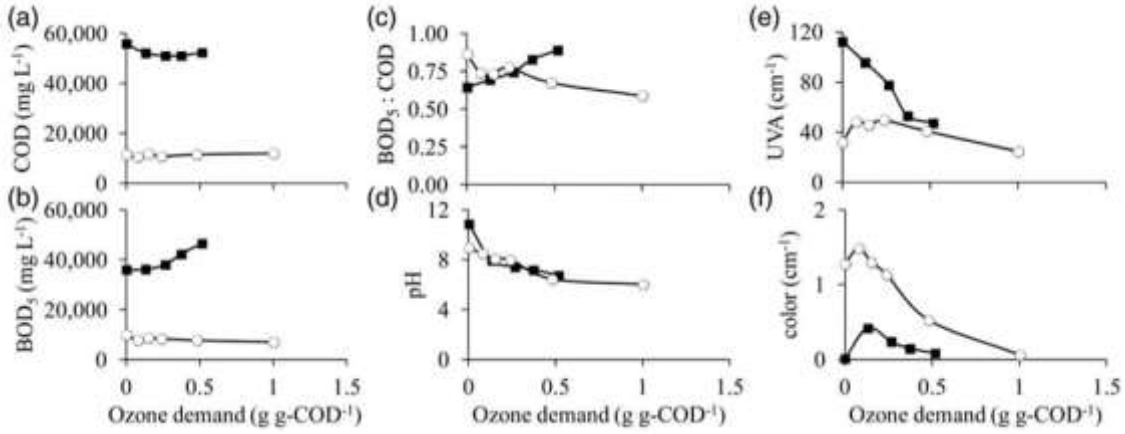


Gram-positive Microthrix sp., which is defined by smooth and thin curves (MBR foam samples), and Gram-positive Nocardia sp., which is defined by short, branching filaments, are both visible under a microscope in the above figure (SBR foam sample).

Ozonation Experiments-

To increase the biodegradability of the effluent, ozonation was tested. On the strong stream or immediately after the biofilter, batch mode implementation was used (choices in the first figure are cf).The findings are shown in the figure below, which suggested that ozone was effective at dis-colouring wastewater and that it also lowered pH and UVA in both the biofilter effluent and the strong stream. The effect on UVA is quite significant, especially as its absorbance is a great predictor of the wastewater's aromatic concentration (Battimelli, 2010). This is also very much the case when there are antibiotics present (Santos &Homem, 2011).Up to an ozone requirement of 0.5g g-COD-1, the strong stream showed the clearest effects of the ozone dosage on UVA. The pre-treatment of bio-refractory substances (melanoidins) found in the effluent from the molasse fermentation industry was also demonstrated to benefit from a comparable ozone dosage (Battimelli et al. 2010).Even though the concentrations of COD were reduced in that research

due to ozonation, COD levels did not change as can be seen in the figure below (a).Additionally, the ozone showed potential in raising the BOD5 of the strong stream seen in the figure below(b), which ultimately led to an improvement in the BOD5: COD ratio increased from 0.64 to 0.89 after a 0.5g g-COD-1 dosage of ozone. However, it did not provide any promising effects when applied to the bio-filter effluent, as can be seen in the picture below (c). Therefore, it is clear that ozonation was most effective when applied to strong streams where it was more selective for bio-refractory chemicals that were reflected by UVA. However, due to the low initial UVA level of the bio-filter wastewater, ozone was ineffective.



The graph displays the impact of ozone demand on the pharmaceutical company's strong stream (strong stream) (■) and bio-filter effluent (○) created in terms of (a) COD (b) BOD5 (c) ratio between BOD5 and COD, (d) pH, (e) UVA, (f) strong stream color.

Conclusions:

The effluent from the pharmaceutical firm, or the antibiotics industry, was treated in the study using a variety of different ways. The SBR and MBR technologies were essential to biological treatment. The MBR obtained greater suspended solid removal while simultaneously the SBR competitiveness as evidenced by the enhanced dissolved UVA removal, particularly at low OLR. But in both situations, the excessive loading rate was accountable for significant foaming which in turn induced the performance loss. It should be noted that the presence of the aromatic compounds may have been detrimental to the growth of the biomass. For this reason, the effectiveness of ozonation pre-treatment was evaluated in a batch trial and exhibited potential when it was applied to the strong stream. Further studies will utilize continuous ozonation to enhance the efficiency of biological pharmaceutical effluent degradation at higher loading rates. The elimination of TDS using physicochemical techniques will also be taken into consideration. Even though they are not permitted to be discharged into the sewage as per the laws, the N and P dosages must also be adjusted to prevent chemical waste.

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