Desalination and Water Treatment
www.deswater.com
doi: 10.5004/dwt.2022.28837

274 (2022) 187–193
October

Competitive removal of tetracycline and paracetamol in the sequencing batch reactor system

Aytekin Celik

Department of Environmental Engineering, Faculty of Engineering, Fırat University, 23119-Elazığ, email: aytekincelik@firat.edu.tr

Received 11 April 2022; Accepted 16 August 2022

ABSTRACT

In this study, removal of both tetracycline (TC) and paracetamol (PCT) were investigated with synthetic wastewater with a sequencing batch reactor. TC and PCT were removed at maximum 62% and 99% under the same conditions which were hydraulic retention time, concentration of dissolved oxygen and acetate concentration, respectively. On the other hand, nitrification and denitrification efficiency were obtained as 95% and 99%. In terms of volumetric removal flux, TC and equivalent O_2 flux of TC were calculated as maximum 2.3 and 4.40 mg/L·d. Likewise, the maximum removal volumetric flux of PCT and its O_2 equivalent flux were determined as 135.9 and 303.1 mg/L·d. The results showed that aerobic bacteria preferred PCT rather than TC.

Keywords: Equivalent flux; Paracetamol; Pharmaceuticals; Sequencing batch reactor; Tetracycline; Volumetric flux

1. Introduction

Pharmaceuticals, personal care products and veterinary pharmaceuticals generally pass through water and wastewater in various ways and from industrial plants. The removal of these pollutants are quite low in classical wastewater treatment plants [1–3]. The widespread existence of pharmaceuticals in the aquatic environment has been alarming for other sectors [1,4,5]. In addition, unused drugs and drugs residuals from waste sludge and drugs from solid waste leaching enter the environment and wastewater treatment plants [6,7].

Although pharmaceuticals such as paracetamol (PCT) are low concentrations in water environments, they can be found in high concentrations in hospital wastewater [8–10]. PCT is a very common pain reliever used as an analgesic, antipyretic drug [11], and used for the treatment of headache, cancer and chronic pains for childrens and adults [12]. In addition to being a good painkiller, PCT can also be used to control brown tree snakes. As there are lots of organisms in the environment and each organism has different sensitivities, pharmaceuticals can be qualified as risk factors for the environment [11]. PCT is a pharmaceutical that is located at the entrance of the wastewater treatment plant and only a small amount can be removed.

Tetracycline (TCs), which are very broad spectrum, are used extensively in the treatment of animal diseases since they are cheap, economical and good antibiotics [13]. However, most of the TC taken into human and animal bodies are excreted from their bodies as metabolites or main products. It is inevitable that these are accumulate over time in aquatic environments and cause toxic effects [14,15]. TC is applied in medicine for its wide pharmaceutical nature and low price. It can also act as a growth agent chemical in waterbond system. TC residues are constantly detected in landfills, soils, and rivers. Excess of TC left in the environment would affect bone growth, irritate the gastrointestinal tract, lead to kidney failure, and other serious diseases in human [16,17]. Therefore, the removal

of TC and PCT have become hot research topic in the current situation.

Recently, sequencing batch reactor (SBR) system has been used to remove organic contaminants and phosphate from wastewater. Excessive nutrient discharges to water systems have made modifications of SBR systems compulsory to achieve nitrification and denitrification. SBR treatment system includes filling, reaction, settling, pouring and preparation steps. There are a lots of studies in the literature on nutrient removal from wastewater. For example, advanced oxidation processes (AOPs) [18–21], adsorption [22], pure bacterial cultures [23], subsurface flow constructed wetlands [24] and anaerobic treatment [25] can be used for PCT removal from wastewater. And also, several methods have been studied to remove pharmaceuticals from wastewater, such as membrane bioreactors [26,27] conventional activated sludges [28,29], moving bed biofilm reactors [30–33]. For example, Sipma et al. [34] reported good removal of pharmaceuticals such as acetaminophen (99% removed), ibuprofen (93% removed), and paroxetine (91% removed) in activated sludge.

In the literature, there have not been any studies on the simultaneous removal of PCT and TC by nitrifying and denitrifying bacteria and toxic effects on these bacteria. In addition, studies on antibiotic removal in the literature are generally chemical and pyhsical treatment methods. PCT and TC are two pharmaceuticals that are very likely to be together in wastewater treatment plants [35]. PCT and TC could be removed by many methods as mentioned above. Among them, biological systems are more suitable treatment systems in terms of economy and health. On the contrary, it has been stated in the literature that phthalic anhydride, which is formed as a result of the biological degradation of tetracycline, is more toxic than tetracycline [36]. However, since dosage is important in toxicity, it is obvious that such molecules do not harm the environment as much as the main molecule. In this context, SBR system was used in this study due to the simultaneous nitrification and denitrification potential, the potential to remove pollutants, small footprint and many treatments were studied in a single reactor. The aim of this study was to show Whether or not PCT and TC pharmaceuticals, were likely to be together in wastewater, were biodegradable more easily in the SBR system.

2. Material and methods

2.1. Operating conditions

Inoculum sample was supplied by the supernatant of activated sludge from a municipal wastewater treatment plant (Malatya, Turkey). The SBR was fed with only 20 mg N/L ammonium at 3 mg/L·O_2 and nitrate with 48 h hydraulic retention time (HRT) in order to form the biomass for acclimatization period of nitrification and denitrification microorganisms for 14 d. After acclimation, the studied periods were applied and removal performance of the TC and PCT were examined in comparison with each other. The SBR system firstly was initiated in aerobic phase and then anaerobic, respectively. Acetate was added as an auxiliary carbon source only in the anaerobic phase (Table 1). In this study, the effects of short circle times on the system were also investigated. In addition, the microorganism concentration was kept between 2,000–3,500 mg/L.

2.2. Chemicals agents

98% tetracycline hydrochloride (CAS No. 2058-46-0) was purchased from AppliChem and Sigma-Aldrich. And also 98% paracetamol (CAS No. AC102332500) was purchased from Acros Organics. 99.9% methanol (CAS No. 67-56-1), 99.8% acetonitrile (CAS No. 75-05-8), and 99.8% formic acid (CAS No. 23-26-45) from Merck were high-performance liquid chromatography (HPLC) grade. Other chemicals, such as sodium chloride (NaCl), sodium sulfate (Na_2SO_4), sodium nitrate ($NaNO_3$), were also ACS grade.

2.3. Medium

SBR system were fed with PCT, ammonium and TC-feeding mediums as synthetic wastewater at room temperature and neutral pH. The composition of medium contained per liter: 0.115 g (NH_4Cl), 0.50 g $NaHCO_3$, 0.13 g

Table 1
Operating conditions in SBR

Periods	Tetracycline concentration, (ppm)	Paracetamol concentration, (ppm)	Times, (d)	Aerobic times in the circle, (h)	Anaerobic times in the circle, (h)	Sodium acetate, (g)	Dissolved oxygen, (ppm)	Anaerobic NO_2–N, (ppm)	Aerobic NO_2–N, (ppm)
P1	0.4–0.5	0.5–0.55	18–33	9	14	0.14	1–2	0.96	1.78
P2	‘’	‘’	33–40	14	9	0.3	4–5	0.17	1.17
P3	‘’	‘’	40–58	9	14	‘’	4–5	0.11	0.17
P4	1–1.1	1.95–2.1	58–68	14	9	0.6	‘’	0.19	0.17
P5	0.95–1	1.95–2.0	68–77	9	14	‘’	‘’	0.06	0.64
P6	0.9–1	1.9–2	77–83	3	5	‘’	‘’	0.01	8.73
P7	‘’	4.9–5	83–88	14	9	‘’	‘’	0.02	0.03
P8	Not feeded	100–110 feeded at aerobic phase	88–98	14	9	0.04	‘’	0.07	0.16
P9	Not feeded	500–515 feeded at anaerobic phase	98–101	12	11	0.04	‘’	0.13	1.35

KH_2PO_4, 0.1 g $MgSO_4 \cdot 7H_2O$, 0.001 g $CaCl_2 \cdot 2H_2O$,0.001 g $FeSO_4 \cdot 7H_2O$, $CH_3COONa \cdot 3H_2O$ and 2 mL trace mineral solution. The trace mineral solution contained per liter: 100 mg $ZnSO_4 \cdot 7H_2O$, 30 mg $MnCl_2 \cdot 4H_2O$, 300 mg H_3BO_3, 200 mg $CoCl_2 \cdot 6H_2O$, 10 mg $CuCl_2 \cdot 2H_2O$, 10 mg $NiCl_2 \cdot 6H_2O$.

2.4. Analytical methods

Samples were taken from influent and effluent were filtered immediately through a 0.22 μm membrane filter prior to TC and PCT analysis's by HPLC (Shimadzu) with an AllureBiPh column (5 μm, 150 mm × 4.6 mm) after taking periodically. The mobile phase was composed of a mixture of ammonium dihydrogen phosphate/acetonitrile (20/80, v/v). Flow rate and injection volume were maintained at 1.2 mL/min and 100 μL, respectively. TC was detected at 269 nm by a diode array detector. The retention time for TC was found to be 4 min.

PCT analysis was performed by HPLC (Shimadzu). In the method, a mixture of methanol/ultrapure water/acetic acid (35/65/0.1, v/v/v) was used as the mobile phase. Flow rate is 0.4 mL/min, detector wavelength is 243 nm and sampling volume is set to 30 μL. The column type is C18 5 μm, 150 mm × 4.6 mm and retention time is 5.31 min.

In addition, NO_3^-, NO_2^-, NH_4^+ analysis were performed by ion chromatograph (IC, Shimadzu). In the method, 2.5 mM phthalic acid (pH = 4) and 2.5 mM oxalic acid were used for the determination of anions and cations, respectively. The column Shim-pack IC-C4 and Shim-pack IC-A1 were also used for anions and cations, respectively. Flow rates were 1 and 1.5 mL/min for cationic and anionic columns. Injection volume was maintained at 50 and 30 μL for cationic and anionic columns. However, the retention time for NH_4^+, NO_2^- and NO_3^- were found to be 4.148, 2.95 and 4 min, respectively.

2.5. PCT and TC mineralization reactions

$$C_{22}H_{24}N_2O_8 + 26.5O_2 \rightarrow 22CO_2 + 11H_2O + 2H^+ + NO_3^- \quad (1)$$

Eq. (1) shows the reaction that occur as a result of complete degradation of TC with O_2.

$$J = \frac{Q \times (C_0 - C)}{V} \quad (2)$$

where J denotes the volumetric removal flux of TC/PCT, C_0 is TC/PCT initial concentration, C is TC/PCT concentration after the reaction time, and V is the modified volume in SBR.

$$J_{O_2\text{-TC}} = 1.91 J_{TC} \quad (3)$$

$$C_8H_9NO_2 + 10.5\,O_2 \rightarrow 8CO_2 + 11H_2O + 2H^+ + NO_3^- \quad (4)$$

Eq. (4) shows the reaction that occur as a result of complete degradation of PCT with O_2 to CO_2 and H_2O.

$$J_{O_2\text{-PCT}} = 2.23\, J_{PCT} \quad (5)$$

3. Results and discussion

In this study, TC and PCT have been removed simultaneously by nitrification and denitrification bacteria in the SBR system. In generally, PCT removal was not affected by the classical conditions and it was over 95% removed. On the contrary, TC was removed by a maximum of 60%. The conditions applied in the study are shown in Table 1. Despite the applied conditions, removal performance of the pollutants were evaluated as below.

3.1. TC mineralization in SBR

Fig. 1a shows the removal performance of TC depending on the conditions in the aerobic phase. In this context, 7 conditions were applied in total.

P1 condition was studied between 18–33 d and maximum TC removal was obtained 53%. At P2 condition, TC removal increased from 53% to 58%. This condition was studied between 33–40 d, dissolved oxygen concentration and HRT in aerobic phase were 4–5 ppm and 14 h, respectively. At P1, the aerobic phase was operated at HRT of 9 h and the concentration of dissolved oxygen between 1–2 ppm in which caused the removal of TC to be lower than P2. A study showed that when TC concentration increased, biological removal efficiency decreased slightly. In addition, it was reported that TC was at most 5%–7% biosorpated in biological removal, and the remaining 50%–70% was biodegradable in SBR [36]. In another study conducted in the same way, it was stated that most of the TC removal was biodegradable [37]. At P3, TC removal was obtained around 20%. And also conditions of P3 and P1 were the same, the removal of TC were determined 53% and 20%, respectively. This status was caused due to the opposite effect of the sudden transition from high to low HRT or the effect of nitrification bacteria not removing with full performance. One aim of trying this condition was to determine the effect of the sudden drop in transition from high to low HRT on removal performance. P4 condition was tried between 58–68 d. In this condition, HRT in the aerobic phase was again increased to 14 h, and TC influent concentration was doubled from 0.5 to 1 ppm. In this context, TC removal increased to around 42%. Increasing TC influent concentration did not have a negative effect on removal. However, the increasing of HRT increased TC removal in the system twice compared to the previous condition. It was clearly determined that complex compounds such as TC required high HRT in the SBR system. At P5, HRT was again reduced to 9 h at 1 ppm TC concentration. The removal performance under this condition was around 45%. Doubling TC concentration had no adverse effect on removal performance.

The transition from P4 to P5 was from 14 h to 9 h HRT. The same situation, despite the transition from P2 to P3, TC removal were obtained 45% and 20% in P5 and P3, respectively. The P6 requirement was operated between 77–83 d. In this condition, the aerobic HRT was reduced to 3 h and the performance of high TC concentration at low HRT was examined. In this period, TC was removed 34%. Finally, HRT was increased again to 14 h and the effect of transition from low to high HRT on TC removal was examined in P7.

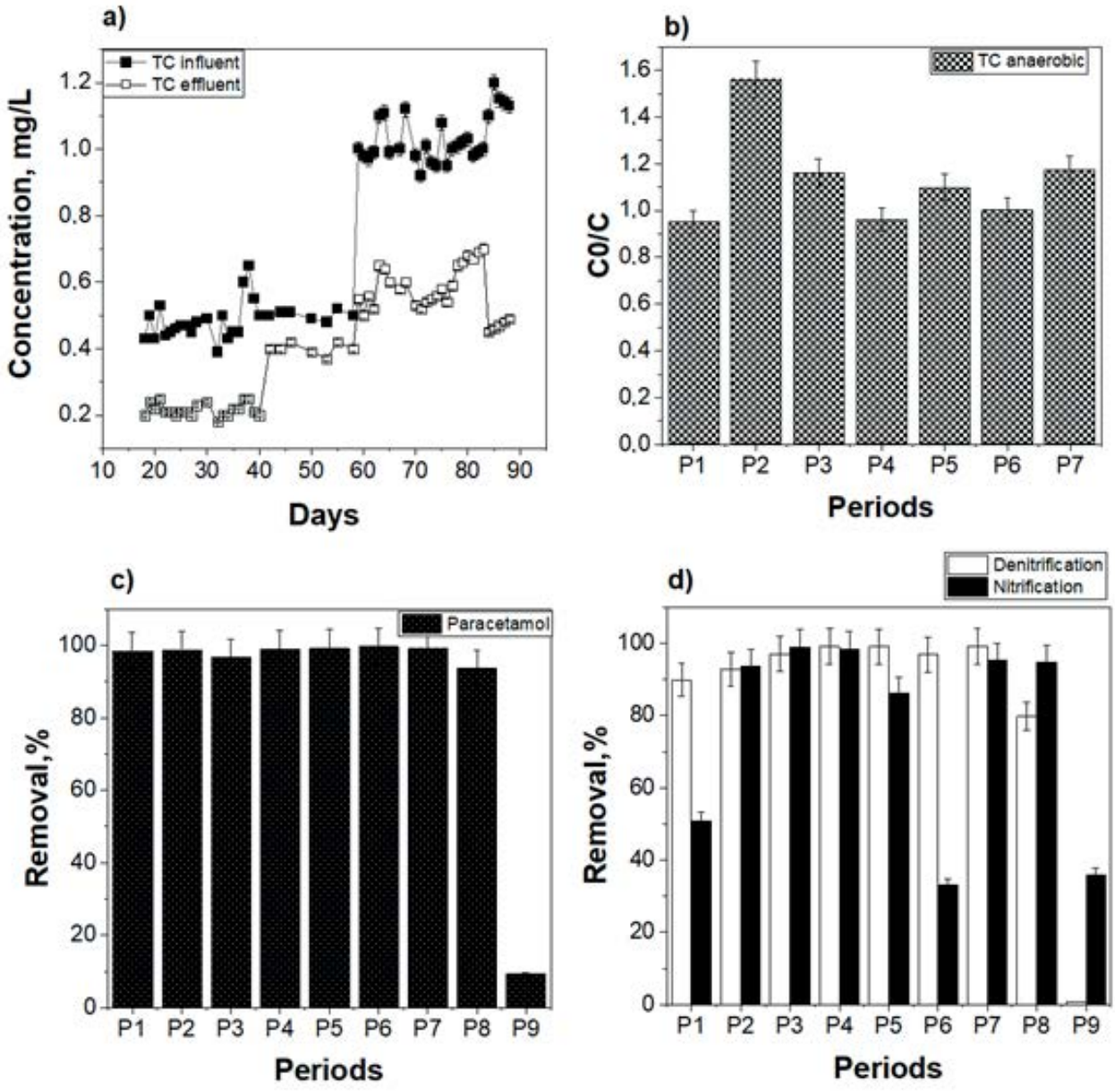

Fig. 1. (a) Removal of tetracycline in aerobic phase in SBR, (b) rate of C_0/C of tetracycline in anaerobic phase, (c) paracetamol removal performance in SBR, and (d) nitrification and denitrification performance in SBR.

Fig. 1b shows the removal performance of TC in the anaerobic phase as C_0/C. In the anaerobic phase, the system was also fed with acetate. Denitrification bacteria did not generally use TC, which was more complex due to acetate feed. When the study was investigated generally, there were only P1 and P4 conditions with C_0/C ratios below 1. This indicated that some of the oxidized TC was reduced to form TC again. The fact that the amount of acetate in P1 was low and the HRT of P4 was high which supported this result. The condition, TC was best removed, P2, it was possible to say that acetate was low and HRT was high. In other periods, the C_0/C ratio changed between 1–1.18. This showed that TC was removed very little due to the acetate feed because acetate has been more easy degradable molecules than tetracycline.

3.2. PCT mineralization in SBR

Fig. 1c shows PCT removal in the SBR system. In this context, 0.5–0.55 ppm of PCT was fed in the first 3 periods, while P4–P6 was fed around 2 ppm. In addition, it was fed approximately 5 ppm in P7, 100–110 ppm in P8 and 500–515 ppm in P9. Although different HRT and different dissolved oxygen concentrations were applied in the first 3 periods, PCT removal was over 96%. In other words, the applied conditions did not affect PCT removal. In addition, it was clearly understood that microorganisms in the aerobic phase accept PCT as carbon source rather than TC. In other words, it can be said that PCT was more easily removed in SBR systems than antibiotics such as TC in aerobic phase.

PCT influent fed concentration between P4 and P6 was increased to 4 times according to the first 3 periods. Despite this situation, PCT removal was obtained again above 96%. Thus, although the HRT was reduced from 9 h to 3 h in P6, PCT removal was not affected in the anaerobic phase. When PCT concentration was increased to 100 ppm in P8, PCT removal could only be reduced to 93%. removal of approximately 100 ppm PCT could only be removed by a chemical treatment such as fenton. In the Fenton process, PCT was fed as 107 ppm and decreased to 5–6 ppm [18]. In addition, approximately 750 ppm PCT was removed by ozonation to meet the exit conditions [19]. This showed the effect of SBR on PCT removal. At P9, influent PCT concentration was increased to 500 ppm, and PCT removal decreased to around 9%. A conclusion made here was that besides aerobic nitrification, there was also a collection of heterotrophic aerobic microorganisms.

3.3. Determination of nitrification and denitrification performance

Fig. 1d shows nitrification and denitrification performance of SBR including TC and PCT depending on the conditions. At P1, nitrification and denitrification performance were determined 50.7% and 89.8%, respectively. Low nitrification in this period resulted from low oxygen delivered to the system. Dissolved oxygen in P1 was measured between 1–2 ppm. By increasing the oxygen given to system in P2, the dissolved oxygen in SBR was increased between 4–5 ppm. This increasing enabled the nitrification to recover immediately and the nitrification efficiency reached around 93%. Denitrification efficiency was high in this condition as before, and it was obtained around 92%. At the same time, acetate was fed to the system at the anaerobic stage during whole operation. Acetate was 0.14 g in P1 and 0.3 g in P2 and P3. In the remaining conditions, acetate was fed as 0.6 g. When the denitrification efficiency was examined according to conditions, it was clearly understood that the appropriate amount of acetate was 0.3 g. The nitrification and denitrification efficiency up to P6 was not adversely affected by the applied conditions and medications, and a yield above 90% was achieved. When the aerobic HRT was reduced to 3 h in P6, the nitrification efficiency decreased to around 33%. The effect of HRT on nitrification clearly has appeared again. Denitrification efficiency was obtained as 97% in P6. In P7, HRT was increased to 14 h, and nitrification efficiency increased again above 95%. Although PCT was increased to 100–110 ppm in P8, nitrification was not significantly affected, and denitrification was around 80%. When the PCT concentration was increased to 500–515 ppm in P9, nitrification and denitrification efficiency were 36% and 0.8%, respectively. The conclusion drawn from this condition was that PCT did not have a significant toxic effect on nitrification and denitrification bacteria up to high concentrations (100–500 ppm). Another result was that denitrification bacteria were more sensitive to PCT than nitrification bacteria.

3.4. Fate of NO_2–N

Table 1 shows the change of nitrite depending on the applied conditions in SBR system in aerobic and anaerobic environment. In the first two conditions, the nitrite concentration formed in the aerobic phase was 1.78 and 1.17 ppm, respectively, while it was 0.96 and 0.17 ppm in the anaerobic phase. NO_2–N formed 0.17, 0.17 and 0.63 ppm in the aerobic phase and 0.11, 0.19 and 0.06 ppm in the anaerobic phase at P3, P4 and P5, respectively. Conditions applied up to P6 provided low concentration of nitrite formation. However, when HRT was reduced to 3 h in the aerobic phase in P6, the nitrite concentration in the aerobic phase was determined as 8.7 ppm due to the low retention time. Under this condition (P6), the formation of nitrite in the anaerobic phase was obtained approximately 0.014 ppm. As HRT was increased again in P7 and P8, nitrite formation in the aerobic phase was formed 0.034 and 0.016 ppm, respectively, while it was 0.018 and 0.07 in the anaerobic phase, respectively. Although the PCT concentration was increased to 100 ppm in P8, nitrite increasing was not observed. This was due to the fact that the PCT fed to the system in P9 increased 500 ppm.

3.5. Determination of performance of TC and equivalent oxygen volumetric flux of TC

TC removal in the aerobic phase as volumetric flux and equivalent oxygen flux were showed in Fig. 2a and b. In P1, the TC flux was 0.55 and the equivalent oxygen flux was approximately 1.02 mg/L·d. The average TC flux and equivalent oxygen flux were obtained 0.48 and 0.95 mg/L·d, respectively in P2. The removal efficiency of P1 was lower than P2, while the flux of P1 was expected to be 1.55 times of P2 due to HRT. It was concluded that both of them have the same effect in terms of load, although the removal efficiency in P2 was high. TC flux was 0.2 and equivalent oxygen flux was 0.41 mg/L·d in P3. In P4, volumetric TC flux was determined to be 0.65 mg/L·d, despite of decreasing in flow rate and the equivalent oxygen flux of TC increased to 1.23 mg/L·d. This was another indication that the removal efficiency in P4 was very good compared to P3. In P5, the TC flux and equivalent oxygen flux were determined 0.88 and 1.83 mg/L·d, respectively. Despite the removal efficiencies in P5 and P4 were the same, the flux in P5 was greater than P4 because of HRT increasing. Although HRT was reduced to 3 h in P6, since the TC removal efficiency did not change much importantly. TC flux and equivalent oxygen flux in this condition (P6) were determined between 1.92–2.3 and 3.67 and 4.4 mg/L·d, respectively. Although removal efficiency in P7 was better despite other conditions, TC and equivalent oxygen flux were 0.91 and 1.79 mg/L·d, respectively. The previous situation has been proven here.

3.6. Determination of performance of PCT and equivalent oxygen volumetric flux of PCT

Fig. 2c and d show the PCT and equivalent oxygen flux in SBR. Since PCT was removed above 95% throughout the study, volumetric PCT and equivalent oxygen flux changed due to the change in flow rate. For example, the PCT flux was 1.27 mg/L·d and the flow rate was 2.13 L/h at P1. But it was 0.77 mg/L·d and the flow rate was 1.37 L/h at P2. As it can be understood from the example, increasing and

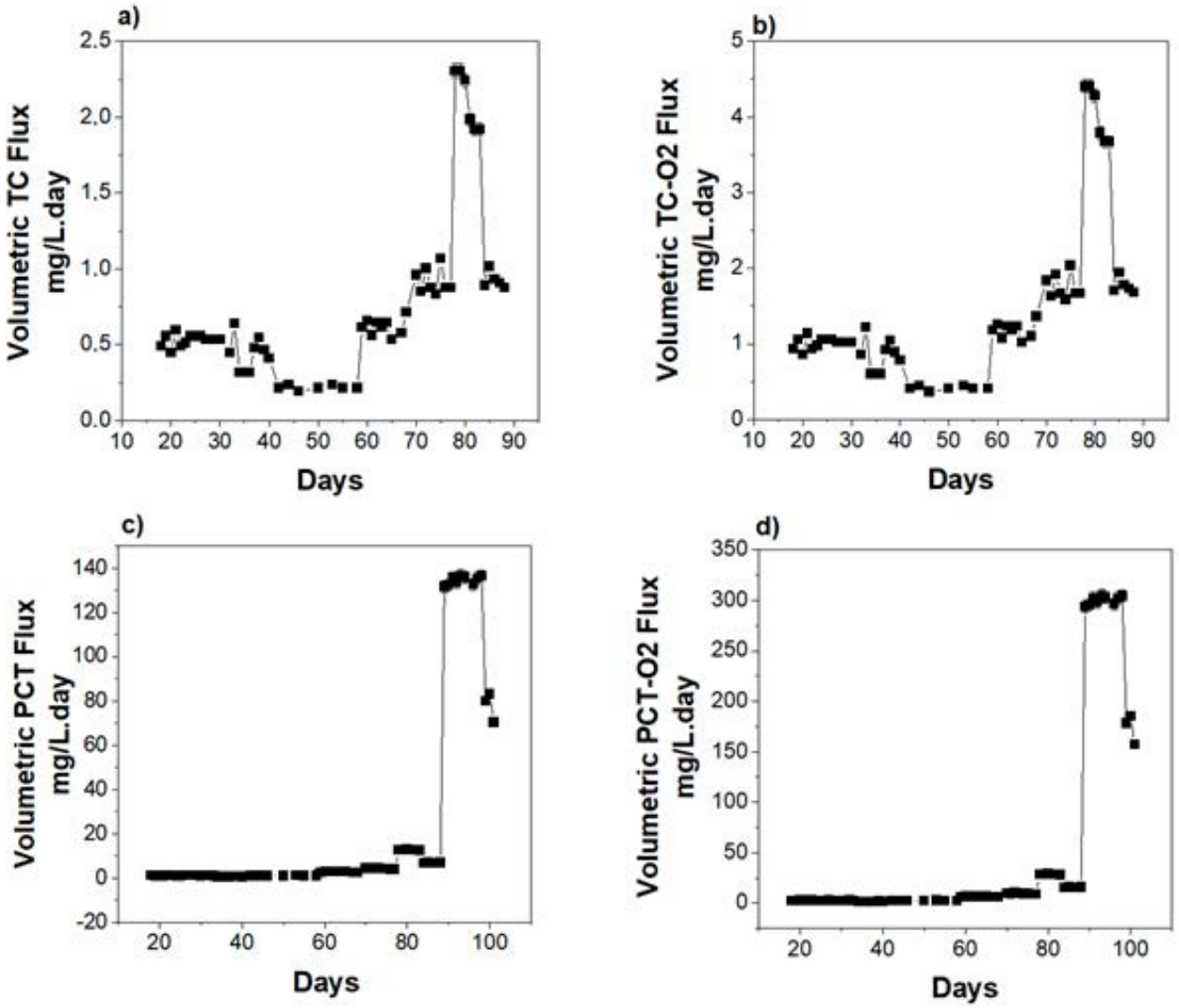

Fig. 2. (a) Volumetric removal flux of tetracycline, (b) volumetric removal of equivalent oxygen of tetracycline flux, (c) volumetric removal flux of paracetamol, and (d) volumetric removal of equivalent oxygen of paracetamol flux.

decreasing in the flow rate changed flux of PCT. In addition, maximum PCT and oxygen equivalent flux were calculated as 130–136 and 295–303 mg/L·d. At P9 condition where PCT was fed as 500 ppm, PCT and oxygen equivalent flux were calculated as 80 and 178 mg/L·d, respectively.

4. Conclusion

Significant conclusions drawn from the study are summarized below.

In this study where tetracycline and paracetamol removal were compared in the SBR system; It was concluded that denitrifying bacteria have more resistant to nitrifying bacteria in PCT and TC removal. In addition, it was determined that microorganisms in the aerobic phase preferred PCT more than TC. It has been shown that more than 95% of PCT can be removed at high HRT in SBR systems. Finally, it has been shown that PCT can be used as an auxiliary carbon source in denitrification processes. It was concluded that future studies should focus on the fate of the biodegradation products of this pharmaceutical formed in the SBR system.

Author contribution

Author (Aytekin CELIK) performed the experiments, the data analysis and wrote the manuscript.

Declarations conflict of interest

The authors declare that they have no conflict of interest.

Ethical statement

The author (Aytekin CELIK) has agreed for authorship, read and approved the manuscript, and given consent for submission and subsequent publication of the manuscript. The manuscript has not been submitted or published anywhere.

Data availability

All data generated or analysed during this study are included in this published article.

References

[1] W. Shi, H. Ren, M. Li, K. Shu, Y. Xu, C. Yan, Y. Tang, Tetracycline removal from aqueous solution by visible-light-driven photocatalytic degradation with low cost red mud wastes, Chem. Eng. J., 382 (2020) 122876, doi: 10.1016/j.cej.2019.122876.

[2] B. Petrie, R. Barden, B. Kasprzyk-Hordern, A review on emerging contaminants in wastewaters and the environment: current knowledge, understudied areas and recommendations for future monitoring, Water Res., 72 (2015) 3–27.

[3] A.V. Flores Nardy Ribeiro, M. Belisário, R. Moretto Galazzi, D. Cazoni Balthazar, M. de Godoi Pereira, J. Nardy Ribeiro, Evaluation of two bioadsorbents for removing paracetamol from aqueous media, Electron. J. Biotechnol., 14 (2011) 7, doi: 10.2225/vol14-issue6-fulltext-8.

[4] A. Rossner, S.A. Snyder, D.R.U. Knappe, Removal of emerging contaminants of concern by alternative adsorbents, Water Res., 43 (2009) 3787–3796.

[5] S.O. de García, G.P. Pinto, P.G. Encina, R.I. Mata, Consumption and occurrence of pharmaceutical and personal care products in the aquatic environment in Spain, Sci. Total Environ., 444 (2013) 451–465.

[6] Y. Yue, Z. Peng, W. Wang, Y. Cai, F. Tan, X. Wang, X. Qiao, Facile preparation of MgO-loaded SiO_2 nanocomposites for tetracycline removal from aqueous solution, Powder Technol., 347 (2019) 1–9.

[7] N. Kulik, M. Trapido, A. Goi, Y. Veressinina, R. Munter, Combined chemical treatment of pharmaceutical effluents from medical ointment production, Chemosphere, 70 (2008) 1525–1531.

[8] M. Gómez-Chaparro, J. García Sanz-Calcedo, L. Armenta-Márquez, Study on the use and consumption of water in Spanish private hospitals as related to healthcare activity, Urban Water J., 15 (2018) 601–608.

[9] M.B. Al Sawaf, F. Karaca, Different stakeholders' opinions toward the sustainability of common textile wastewater treatment technologies in Turkey: a case study Istanbul Province, Sustainable Cities Soc., 42 (2018) 194–205.

[10] A.G. González, J. García-Sanz-Calcedo, D.R. Salgado, Quantitative determination of potable cold water consumption in German hospitals, Sustainability, 10 (2018) 932, doi: 10.3390/su10040932.

[11] I. Sirés Sadornil, Electrochemical Advanced Oxidation Processes for the Removal of the Drugs Paracetamol, Clofibric Acid and Chlorophene from Waters, Universitat de Barcelona, 2007.

[12] Y. Zhu, X. Quan, F. Chen, X. Fan, Y. Feng, CeO_2–TiO_2 coated ceramic membrane with catalytic ozonation capability for treatment of tetracycline in drinking water, Sci. Adv. Mater., 4 (2012) 1191–1199.

[13] C. Yan, Y. Yang, J. Zhou, M. Liu, M. Nie, H. Shi, L. Gu, Antibiotics in the surface water of the Yangtze Estuary: occurrence, distribution and risk assessment, Environ. Pollut., 175 (2013) 22–29.

[14] J.P. Bound, N. Voulvoulis, Pharmaceuticals in the aquatic environment—a comparison of risk assessment strategies, Chemosphere, 56 (2004) 1143–1155.

[15] K. Kümmerer, Antibiotics in the aquatic environment–a review–part II, Chemosphere, 75 (2009) 435–441.

[16] Y. Gao, Y. Li, L. Zhang, H. Huang, J. Hu, S.M. Shah, X. Su, Adsorption and removal of tetracycline antibiotics from aqueous solution by graphene oxide, J. Colloid Interface Sci., 368 (2012) 540–546.

[17] Q. Chang, A. Ali, J. Su, Q. Wen, Y. Bai, Z. Gao, Simultaneous removal of nitrate, manganese, and tetracycline by *Zoogloea* sp. MFQ7: adsorption mechanism of tetracycline by biological precipitation, Bioresour. Technol., 340 (2021) 125690, doi: 10.1016/j.biortech.2021.125690.

[18] G. Dalgic, I.F. Turkdogan, K. Yetilmezsoy, E. Kocak, Treatment of real paracetamol wastewater by Fenton process, Chem. Ind. Chem. Eng. Q., 23 (2017) 177–186.

[19] R. Andreozzi, V. Caprio, R. Marotta, D. Vogna, Paracetamol oxidation from aqueous solutions by means of ozonation and H_2O_2/UV system, Water Res., 37 (2003) 993–1004.

[20] Q.-P. Isariebel, J.-L. Carine, J.-H. Ulises-Javier, W. Anne-Marie, D. Henri, Sonolysis of levodopa and paracetamol in aqueous solutions, Ultrason. Sonochem., 16 (2009) 610–616.

[21] C.-C. Su, L.M. Bellotindos, A.-T. Chang, M.-C. Lu, Degradation of acetaminophen in an aerated Fenton reactor, J. Taiwan Inst. Chem. Eng., 44 (2013) 310–316.

[22] A. Macías-García, J. García-Sanz-Calcedo, J.P. Carrasco-Amador, R. Segura-Cruz, Adsorption of paracetamol in hospital wastewater through activated carbon filters, Sustainability, 11 (2019) 2672, doi: 10.3390/su11092672.

[23] Y. Deng, Y. Zhang, Y. Gao, D. Li, R. Liu, M. Liu, H. Zhang, B. Hu, T. Yu, M. Yang, Microbial community compositional analysis for series reactors treating high level antibiotic wastewater, Environ. Sci. Technol., 46 (2012) 795–801.

[24] E. Ranieri, P. Verlicchi, T.M. Young, Paracetamol removal in subsurface flow constructed wetlands, J. Hydrol., 404 (2011) 130–135.

[25] Y. Li, Y. Gong, H. Zhao, J. Gu, Z. Wang, X. He, Enhancement of chlortetracycline biodegradation with *Trichoderma harzianum* LJ245 and its spore-producing mutants using co-metabolism, Biodegradation, 31 (2020) 265–273.

[26] L. Kovalova, H. Siegrist, H. Singer, A. Wittmer, C.S. McArdell, Hospital wastewater treatment by membrane bioreactor: performance and efficiency for organic micropollutant elimination, Environ. Sci. Technol., 46 (2012) 1536–1545.

[27] I. Vergili, U. Golebatmaz, Y. Kaya, Z.B. Gönder, H. Hasar, G. Yilmaz, Performance and microbial shift during acidification of a real pharmaceutical wastewater by using an anaerobic sequencing batch reactor (AnSBR), J. Environ. Manage., 212 (2018) 186–197.

[28] E. Aubertheau, T. Stalder, L. Mondamert, M.-C. Ploy, C. Dagot, J. Labanowski, Impact of wastewater treatment plant discharge on the contamination of river biofilms by pharmaceuticals and antibiotic resistance, Sci. Total Environ., 579 (2017) 1387–1398.

[29] A. Celik, Oxytetracycline and paracetamol biodegradation performance in the same enriched feed medium with aerobic nitrification/anaerobic denitrification SBR, Bioprocess Biosyst. Eng., 44 (2021) 1649–1658.

[30] M.E. Casas, R.K. Chhetri, G. Ooi, K.M.S. Hansen, K. Litty, M. Christensson, C. Kragelund, H.R. Andersen, K. Bester, Biodegradation of pharmaceuticals in hospital wastewater by staged moving bed biofilm reactors (MBBR), Water Res., 83 (2015) 293–302.

[31] B. Taşkan, Ö. Hanay, E. Taşkan, M. Erdem, H. Hasar, Hydrogen-based membrane biofilm reactor for tetracycline removal: biodegradation, transformation products, and microbial community, Environ. Sci. Pollut. Res., 23 (2016) 21703–21711.

[32] E. Aydın, M. Şahin, E. Taşkan, H. Hasar, M. Erdem, Chlortetracycline removal by using hydrogen based membrane biofilm reactor, J. Hazard. Mater., 320 (2016) 88–95.

[33] A. Celik, M.S. Tunc, O. Hanay, E. Taskan, H. Hasar, Comprehensive evaluation of autohydrogenotrophic membrane biofilm reactor treating OTC-enriched water medium, Bioprocess Biosyst. Eng., 41 (2018) 1261–1269.

[34] J. Sipma, B. Osuna, N. Collado, H. Monclús, G. Ferrero, J. Comas, I. Rodriguez-Roda, Comparison of removal of pharmaceuticals in MBR and activated sludge systems, Desalination, 250 (2010) 653–659.

[35] C. Miège, J.M. Choubert, L. Ribeiro, M. Eusebe, M. Coquery, Removal efficiency of pharmaceuticals and personal care products with varying wastewater treatment processes and operating conditions–conception of a database and first results, Water Sci. Technol., 57 (2008) 49–56.

[36] H. Liu, Y. Yang, H. Sun, L. Zhao, Y. Liu, Fate of tetracycline in enhanced biological nutrient removal process, Chemosphere, 193 (2018) 998–1003.

[37] B. Taşkan, E. Casey, H. Hasar, Simultaneous oxidation of ammonium and tetracycline in a membrane aerated biofilm reactor, Sci. Total Environ., 682 (2019) 553–560.