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Research Article

An investigation based on removal of ibuprofen and its transformation products by a batch activated sludge process: A kinetic study

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ABSTRACT

Ibuprofen metabolites can form in humans as a result of metabolic activities or can be produced by microorganisms in wastewater treatment plants and receiving environments, which increases their likelihood of being present in the environment. In this study, various experiments were conducted to determine the removal degree for ibuprofen, ibuprofen carboxylic acid (IBU-CBX), and 2-hydroxylated ibuprofen (IBU-2-OH) metabolites with an activated sludge reactor. Furthermore, the pseudo-first-order biodegradation rate constant (k_{biol}) (17.76 L/gSSday) was calculated to determine the decomposition degree of ibuprofen in the batch activated sludge system. The effects of different ibuprofen concentrations (8.2, 5.6, 3.2, 1.51 mg/L) at constant biomass concentration (3 g/L) on the biodegradation mechanism were investigated. In addition, IBU-2-OH and IBU-CBX were tested in a batch activated sludge reactor with a volume of 2 L individually at 100 µg/L with activated sludge containing 3 g/L biomass. It was observed that ibuprofen had a removal efficiency of more than 90%. IBU-CBX and IBU-2-OH were removed at approximately 27–91% and 18–82%, respectively. In abiotic conditions, the removal of ibuprofen was found to be 7.07%. It was confirmed that the removal of ibuprofen largely depended on biological degradation. This study enabled us to know which metabolites are involved in the biodegradation process of ibuprofen in batch experiments with the activated sludge process.

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INTRODUCTION

Due to the rapid increase in the human population and technological developments, toxic substance concentrations discharged to the receiving environment increase day by day. Industrial wastewater may contain various organic or inorganic contaminants [1]. Pharmaceutical compounds and their metabolites are subclasses of organic pollutants usually detected in wastewater and surface water. As a result of human consumption and veterinary usage, pharmaceutical compounds are found in wastewater treatment plant effluents, in aquatic environments such as rivers and surface waters, and the potential for these substances to cause adverse effects in the aquatic environment has raised increasing concern [2–6]. The most common way medicines are transmitted to aquatic environments is by discharge from

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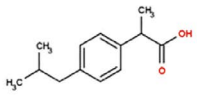
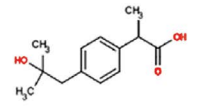
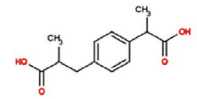
the body due to human consumption, reaching the sewage system and then wastewater treatment plants and from there to drinking water [7]. Many pharmaceutical compounds found in wastewater and processed in wastewater treatment plants are converted into metabolites or are eliminated at low rates or not at all due to their chemical structure [8, 9].

Ibuprofen is one of the most commonly used oral analgesics and antipyretics and is widely used to treat rheumatic disorders, pain, and fever [10, 11]. Moreover, up to 85% of ibuprofen taken into the body is excreted through urine and faeces without being metabolized [12]. It has slight solubility in aqueous solutions and high mobility in the marine environment [13]. It was reported that ibuprofen was detected in wastewater treatment plant effluents at concentrations between 60 ng/L and 100 µg/L in different countries [10, 14]. Therefore, there is increasing research interest in the biotransformation of ibuprofen during biological wastewater treatment processes [15, 16]. Many methods are used for the removal of pharmaceutics from aquatic environments, such as anaerobic digestion [17], phytoremediation [18], biodegradation by pure cultures [19], moving bed biofilm reactor (MBBR) [20], and adsorption [21, 22]. Also, advanced oxidation methods [23] are used, such as electro Fenton [24] and photodegradation [25]. Physicochemical methods have disadvantages such as high operating costs and the formation of secondary pollutants [26]. Although biological treatment processes have some disadvantages, such as the adaptation of microorganisms to the environment and the need for long hydraulic retention times for the biological degradation of pharmaceuticals, it is considered an environmentally friendly option due to its low-cost operating requirements and harmless end products generation [27].

The main mechanisms in biological removal are biotransformation, degradation, and adsorption [28–30]. It is possible to examine the mechanism in biological processes with kinetic models. Some studies investigated the biotransformation removal data with pseudo-first-order and pseudo-second-order kinetic models [31, 32]. For biodegradation processes of pharmaceutical compounds in activated sludge, it was proposed to use pseudo-first-order reaction kinetics and biodegradation reaction rate constants (k_{biol}) [33]. Due to biodegradation and sorption processes, ibuprofen has a high removal efficiency (about 90%) in wastewater treatment plants [34]. Many studies investigate ibuprofen biodegradation in wastewater treatment plant inlet and outlet waters and lab-scale batch experiments [35, 36]. 2-hydroxy ibuprofen (IBU-2-OH) and carboxyibuprofen (IBU-CBX) are the main ibuprofen metabolites in humans. 1-hydroxy ibuprofen (IBU-1-OH), 3-hydroxy ibuprofen (IBU-3-OH) and phase II metabolites can be found at low concentrations in urine. Zwiener et al. (2002) [35] reported that ibuprofen converts to IBU-CBX and IBU-2-OH under oxic conditions and only IBU-CBX under anoxic conditions in their study. Quintana et al. (2005) [37] found that IBU-2-OH was produced before IBU-1-OH in a membrane bioreactor, and both were quickly removed from the bioreactor. This study aims to investigate the removal of different concentrations of ibuprofen and its metabolites in a batch activated sludge process, which is widely used for organic matter removal. Not only ibuprofen but also its metabolites were monitored during the biodegradation process by liquid chromatography-mass spectrometry/mass spectrometry (LC-MS/MS) chromatography. Moreover, the data obtained were used with the well-known kinetic models to examine the removal mechanism of ibuprofen during the activated sludge process.

Table 1. Physico-chemical properties of ibuprofen, IBU-2-OH, and IBU-CBX [40]

Compound	Structure	pKa	LogKow
Ibuprofen		4.91	3.97
IBU-2-OH		4.55	2.69
IBU-CBX		3.97	2.78

Some studies have mentioned the toxic effects of ibuprofen and its metabolites. It has been reported that ibuprofen may cause acute toxicity to aquatic organisms at various concentrations and may cause a long-term ecological impact on non-target organisms if discharged continuously into the receiving environment [38]. It has also been reported that the excretion product may contain both ibuprofen and its metabolites, and its metabolites may be more toxic than its parent molecule [39]. To the authors' best knowledge, studies supporting the biodegradation of high concentrations of ibuprofen and its conversion products (TPs) are limited and need further investigation.

MATERIALS AND METHODS

Chemicals and Compound Selection

NaOH (CAS Number: 1310-73-2) and HCl (CAS Number: 7647-01-0) were purchased from Sigma-Aldrich and used in pH settings through the trials. Sodium azide (NaN_3) was purchased from Sigma-Aldrich (CAS Number: 26628-22-8) and used to inhibit the activated sludge activity. Ibuprofen, IBU-2-OH, and IBU-CBX were supplied by Sigma Aldrich, and HPLC grade was provided by Merck (Germany). Physicochemical properties of the pharmaceutical compounds should also be considered to estimate their biodegradation potential. Calibration

Table 2. Gradient conditions for IBU-2-OH and IBU-CBX (a- Solvent Composition b-Timetable)

a) Solvent Composition

	Chanel	Ch.1 Solv.		Name 1	Used	Percent
1	A	100% Water	0.1	Ammonium Formate (pH:5.5, Formic Acid)	Yes	90%
2	B	100% Methanol			Yes	100%
3	C				No	
4	D			0.1% Formic Acid	No	

b) Timetable

	Time(min)	A	B	C	D
1	1	90%	10%	0%	0%
2	1.10	0%	100%	0%	0%
3	4.00	0%	100%	0%	0%
4	4.10	90%	10%	0%	0%

standard solutions were prepared by diluting the stock solution of the target compounds appropriately in methanol-water (10:90, v/v). Table 1 shows the physicochemical properties and molecular structures of ibuprofen and its metabolites [40].

Analytical Methods

Solid-phase extraction (SPE) was applied to samples taken from batch-operated reactors using a method developed by Gros et al. (2012) [14]. For the solid phase extraction process, 60 mg OASIS HLB (Waters, USA), cartridges with 5 mL of methanol and 5 mL of ultrapure water pH adjusted to 4.5 were pre-conditioned. Afterward, 30 mL of wastewater was loaded into the cartridge at a 10 mL/min loading rate. The cartridge was washed with 3 mL of 2% methanol solution at a 5 mL/min rate to separate the substances likely to adhere to the pharmaceutical compound from the cartridge and then dried under vacuum for 15 min. Finally, the recovery process was applied with methanol at a rate of 1 mL/min. Both biodegradation and adsorption of ibuprofen in aqueous environments were analyzed by Agilent 1100 Model HPLC device. In the HPLC analysis, a chromacil 100-5-C18 column with 250x4.6 mm, 4 µm particle diameter was used, and the flow rate was determined as 1.0 mL/min. The mobile phase was separated with a binary mobile phase at a 0.4 mL/min flow rate using pH=8 (A) and 5 mM of methanol (B) and ammonium acetate. The analysis was carried out at 220 nm wavelength and 25 °C separation temperature. Chromatographic separation for biological degradation of IBU-2-OH and IBU-CBX was performed with Agilent Technologies 1290 Infinity model UPLC equipped with a quaternary pump system (Mildford, USA) using a Zorbax Eclipse C18 column (50 mm x 2.91 mm id 1.8 µm). Agilent Technologies 6460 Triple Quad LC-MS/MS system was used as the detector. Sample injection volume was determined as 5 µL. Gradient conditions for IBU-2-OH and IBU-CBX are given in Table 2. System efficiency was calculated with chemical oxygen demand (COD) removal during the acclimatization of activated sludge to ibuprofen. The COD value of the wastewater was analyzed with a spectrophotometer (WTW spectroflex 6100, at 600 nm wavelength) according to the closed reflux colorimetric method [41].

Synthetic Wastewater and Acclimation Period

Activated sludge was aerated to maintain aerobic conditions by feeding it with synthetic wastewater prepared according to ISO11733 standard (Table 3) [42]. The pH was adjusted to about 7.0 with 0.2 M HCl or 0.2 M NaOH. The wastewater fed into the system for one day after a 12-day acclimatization period. In order to acclimatize the activated sludge biomass, ibuprofen active ingredient was fed into activated sludge for 12 days with synthetic wastewater containing 550 mg/L COD. It is provided COD / N / P as 100 / 5 / 1 to allow the growth of microorganisms. During the studies, the wastewater was prepared daily to prevent changes in the composition of synthetic domestic wastewater. After acclimatization, COD removal was determined as 90% that showed activated sludge and bacteria adapt to the new environment. Sludge retention time

Table 3. Synthetic wastewater composition prepared according to ISO11733 Standard [42]

Content	
Peptone	192 mg/L
Meat extract	138 mg/L
Glucose monohydrate	19 mg/L
Ammonium chloride (NH_4Cl)	23 mg/L
Anhydrous potassium monohydrogen phosphate (K_2HPO_4)	16 mg/L
Disodium hydrogenphosphate dihydrate ($Na_2HPO_4.2H_2O$)	32 mg/L
Sodium hydrogen carbonate ($NaHCO_3$)	294 mg/L
Sodium chloride (NaCl)	60 mg/L
Iron (III) chloride hexahydrate ($FeCl_3.6H_2O$)	40 mg/L

(SRT) was operated for 10 days and hydraulic retention time (HRT) 24 h in the activated sludge reactor. During the acclimation period, ibuprofen at a concentration of 1mg/L was given to the batch activated sludge process with synthetic wastewater, and the MLSS concentration was kept at 3 g/L.

Biodegradation Studies

To investigate the biodegradation and removal of ibuprofen and its metabolites, a study was carried out in a system operated intermittently in the laboratory with activated sludge from a domestic wastewater treatment plant. Activated sludge used in the study was taken from the Edremit Municipality domestic wastewater treatment plant operating in Van province in Turkey. Edremit advanced biological wastewater treatment plant is designed to serve an equivalent population of 100,000 people and a maximum flow rate of 21.840 m^3/day. It is located between 345904 latitudes and 4253273 longitudes. The treatment plant is operated as HRT 48 hours and SRT 20 days.

Batch experiments were carried out in 3 batch reactors (250 mL glass flask) with continuous stirring at room temperature (20 °C ± 2 °C), keeping dissolved oxygen constant at approximately 6.4 mg O_2/L and filled with 100 mL of activated sludge. These values appear to be significantly higher than the dissolved oxygen measured in the actual WWTP activated sludge process. Because dissolved oxygen is kept at this value to eliminate the decrease in non-aerated areas in lab-scale activated sludge processes. Other studies keep dissolved oxygen levels close or higher than in this study. To prevent anaerobic reactions, the dissolved oxygen concentration should be kept above 2 mg/L [43, 44]. Ferrando-Climent et al. (2012) [40] kept the dissolved oxygen level constant at 7.5 mg/L in their study in batch activated sludge reactors.

After the biomass acclimatization process, pharmaceutical compounds were added to the synthetic wastewater at different concentrations for a period equal to SRT 10.

Biodegradation rates may vary depending on differences in initial charge of the compound or sludge composition and experimental conditions [31]. To determine the k_{biol} coefficient, samples were taken at 20 min intervals for 1 h, and the inlet and outlet concentrations were determined. The k_{biol} values of the activated sludge process generally vary between 9–35 L/gSSday [45].

Experiments were carried out in two sets. The first experiment set investigated the effect of different ibuprofen concentrations (8.2, 5.6, 3.2, 1.51 mg/L) at constant biomass concentration (3 g/L). In a second experiment set, IBU-2-OH and IBU-CBX were added separately at 100 µg/L to another activated sludge reactor containing 3 g/L biomass. The system was operated at room temperature. 10 mL samples were taken at different time intervals (0.83,0.25,0.5,1,2,3,4,5,6 h) from each reactor, and after centrifugation (10 min at 5000 rpm), the supernatant liquid was stored in a refrigerator at 4 °C. Before analysis, liquid samples were homogenized using a vortex. Ibuprofen concentration was determined using Agilent 1100 Model HPLC and 1290 Infinity model UPLC and its metabolites were determined using Agilent Technologies 6460 Triple Quad LC-MS/MS.

Adsorption and Kinetic Studies

Adsorption trials with inactivated sludge were carried out to investigate the removal of ibuprofen under abiotic conditions. The experiments were performed in triplicate. In visualized data error bar shows the standard deviation with three replicates. Inactivated sludge was used to understand the role of the adsorption process, as well as biodegradation, in the ibuprofen removal mechanism. The activity of activated sludge was inhibited using NaN_3 (0.1%, w/v) [46]. The samples taken at different time intervals (5–1440 min.) under abiotic conditions were analyzed for ibuprofen removal. Batch reactors were wrapped in aluminum foil to prevent photodegradation of pharmaceutical compounds and placed in a shaker at 200 rpm.

Contact time is critical to discuss the adsorption mechanisms [47] and equilibrium time in more detail. This study investigates the effect of contact time depending on the relationship between the inactivated sludge and the ibuprofen. Kinetic studies were carried out at an initial ibuprofen concentration of 8.2 mg/L for 5 to 1444 min, inactivated sludge dose (m) of 2 g, and volume of 100 mL, the temperature of 25 °C, 200 rpm stirring speed, and wastewater pH (natural) of 7.35. The experimental data obtained were applied to well-known kinetic models represented by Eqs. (1), (2), (3), and (4) to define the degree of adsorption, such as intraparticle diffusion, Elovich, pseudo-first-order, and pseudo-second-order [48, 49].

$$q_t = k_{id} t^{\frac{1}{2}} + C \quad (1)$$

k_{id} refers to the intra-particle diffusion rate constant (mg/g.min$^{1/2}$). The slope of the line obtained from the graph of q_t against $t^{1/2}$ gives k_{id}, and the intersection gives *C*. *C* gives the experimenter an idea of the boundary layer thickness [50].

β (g/mg) and α (mg/g.min) represent Elovich rate constants and can be calculated from the intersection point and slope of the line β and α by plotting q_t against $t^{1/2}$.

$$q_t = \frac{1}{\beta}\ln\alpha\beta + \frac{1}{\beta}\ln t \quad (2)$$

$$\log(q_e - q_t) = \log q_e - \frac{k_1}{2.303} t \quad (3)$$

$$\frac{t}{qt} = \frac{1}{k_2 q_e^2} + \left(\frac{1}{q_e}\right) t \quad (4)$$

q_t and q_e are the amount (mg/g) of ibuprofen adsorbed at t and equilibrium, respectively. k_1 (min^{-1}) is the first-order adsorption rate constant and k_2 (g/mg.min) is the second-order adsorption rate constant. From the line obtained by plotting *t* against log (q_e - q_t), k_1 and q_e values can be calculated from slope and intersection, respectively. From the slope and intersection of *t* 'against t/q_t, k_2 and q_e can be calculated, respectively.

RESULTS AND DISCUSSION

Biodegradation studies

Biodegradation of Ibuprofen in Batch Activated Sludge System

Since ibuprofen has a low Henry constant (6.10E–06 atm m^3/mol), the loss due to evaporation is negligible [51]. The most important degradation mechanisms for ibuprofen are sorption into sludge and biodegradation. Aerobic batch experiments were performed in an activated sludge reactor containing different concentrations of ibuprofen and constant biomass. The time-dependent variation of the different ibuprofen concentrations is shown in Figure 1.

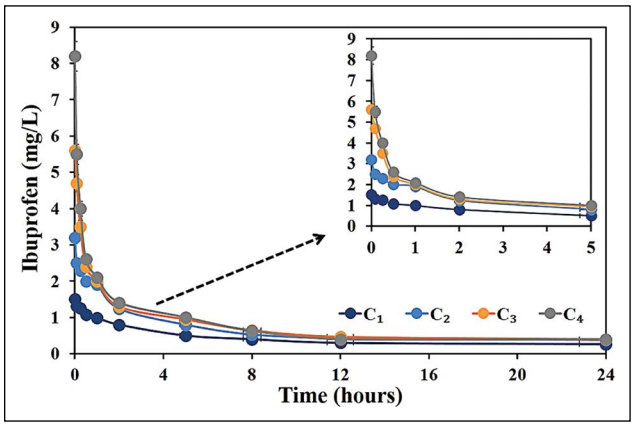


Figure 1. Time-dependent variation of different ibuprofen concentrations in the batch activated sludge reactor.

As the enzyme concentration will increase at high biomass amounts such as 3 g/L, the reaction rate depends on the enzyme concentration; the substrate/enzyme ratio will decrease as the amount of enzyme increases with the fixed substrate value [7]. Suarez et al. (2010) [52] worked in 2 L bioreactors and achieved removal efficiency above 80% in aerobic conditions and below 20% in anoxic conditions. As seen in Figure 1, it was observed that ibuprofen at different concentrations was removed at approximately the same time (2 h). Similar to these results, Collado et al. (2012) [31] found that the degradation efficiency for ibuprofen was higher when the same initial biomass concentration was used and at low ibuprofen concentrations. Furthermore, Quintana et al. (2005) [37] observed that ibuprofen biodegradation was rapid, which is in good agreement with our results. This study investigated the effectiveness of ibuprofen active substance added to synthetic wastewater in different concentrations. It was observed that ibuprofen was removed at 90–95% in approximately 24 h (Fig. 1). As can be seen from the trials conducted at a constant biomass concentration of 3 g/L, 90% removal is possible in 12.5 h (0.52 day), and ibuprofen removal efficiency was observed at up to 95% in 14–24 h (0.6–1 day). In this case, although 0.7 mg/L ibuprofen was used during the 12-day acclimatization period, microorganisms in the wastewater successfully tolerated the applied ibuprofen concentrations. Hijosa-Valsero et al. (2010) [53] reported 40% efficiency for ibuprofen in the activated sludge system. Furthermore, in another study using a sequential batch membrane bioreactor, removal efficiency in the range of 50–90% was reported for ibuprofen [54].

Calculation of the Biological Degradation Constant (k_{biol})

Kinetic modeling should be considered to develop appropriate mathematical models to predict the performance of treatment systems. One of the most important ways to understand the removal mechanism better is to evaluate the

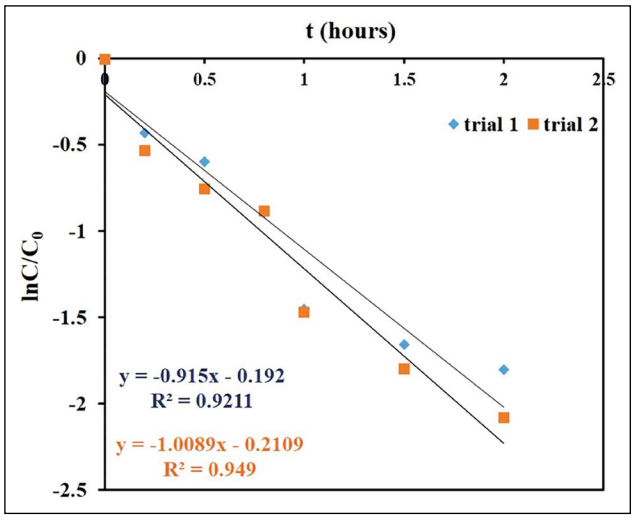


Figure 2. Change in biodegradation of ibuprofen versus time during batch experimental studies.

kinetic data. To understand the mechanism controlling the biological process, a pseudo-first-order kinetic model that aims to examine the removal process of ibuprofen was used. Since pharmaceutical compounds are present in very low concentrations, a first-order model is used that the biomass concentration and the soluble concentration of the pollutant affect the rate of biodegradation.

The change in biodegradation of ibuprofen obtained in experimental studies over time is shown in Figure 2.

The concentration of a pharmaceutical compound in wastewater can be modelled according to the pseudo-first-order kinetic model as follows [33, 36].

$$\frac{C_i}{C_o} = e^{-k_{biol}*SS*HRT} = e^{-k_{biol}*SP*SRT} \quad (5)$$

Where;

C_i: Inlet ibuprofen concentration (µg/L)

C_o: Output ibuprofen concentration (µg/L)

HRT: Hydraulic retention time for the entire reactor or duration of the batch reactor (day)

SP: Specific sludge production per volume of treated wastewater (gSS/m^3 wastewater)

SS: Suspended solids concentration

SRT: Sludge age (day)

k_{biol}: Pseudo-first-order degradation constant

Converting Eq. (5) to linear form gives Eq. (6).

$$ln\frac{C_i}{C_o} = -k_{biol} * SS * HRT \quad (6)$$

The slope of the line obtained by plotting the ln (C_i/C_0) value against time will give -k_{biol} * SS value.

k_{biol} is a vital parameter widely used in the literature to compare the removal efficiency of compounds in many micropollutant classes such as ibuprofen [55]. In aerobic batch experiments, studies were conducted to establish a relationship between pharmaceutical compounds' biological kinetic degradation coefficient and removal capacity. The following information gives this relation [56].

- If k_{biol} <0.1 [L/gSS.day]: No removal (less than 20%)
- If 0.1 <k_{biol} <10: partial removal up to 20–90%
- k_{biol} >10: More than 95% removal due to biodegradation and largely reactor configuration.

To calculate k_{biol} (L/gSSday), the slope of the line in Figure 2 was divided by the MLSS concentration of activated sludge and multiplied by 24 h. MLSS was used as an estimate of the biomass concentration found in the activated sludge reactor. The MLSS concentration of the batch activated sludge reactor is 3 g/L on average.

In this study, the k_{biol} value obtained for ibuprofen was obtained as 17.76 L/gSSday. The biodegradation mechanism seems to be essential for the removal of ibuprofen, depending on the k_{biol} value. In other words, it can be said that the removal of ibuprofen is between 90–95% by biological degradation. A similar result was reported by Smook et al. (2008) [36]. Moreover, Kruglova et al. (2014) [57] found the k_{biol} value for ibuprofen was 10 L/gSS day. Based on this value, he interpreted that ibuprofen is an easily biodegradable chemical substance [57]. The comparison of the k_{biol} value calculated in this study and the literature is given in Table 4. According to Table 4, the k_{biol} value we obtained for ibuprofen was found to be similar to some experimental studies, and ibuprofen can be considered as a biodegradable pharmaceutical due to its high k_{biol} values [57]. The difference between these experiments and those reported in the literature is the pharmaceutical compound concentration. This difference in biodegradation constant is likely due to differences in wastewater and wastewater treatment plant, such as sludge age, wastewater inlet characteristics, flow chart of the relevant treatment plants, and experimental methods used. The k_{biol} values obtained in this study are lower than those found in the literature. The lower k_{biol} values in laboratory-scale plants compared to full-scale plants can be explained by a lower SRT. In other words, as the biomass concentration decreases, the k_{biol} value decreases [31].

High removal efficiencies were observed with increasing SRT in general [59]. However, compounds with high k_{biol} values, such as ibuprofen and paracetamol can be nearly removed entirely by biodegradation independently of SRT and HRT [60]. SRT is an important parameter for both sorption and biological degradation. In this study, SRT was selected as 10 days and HRT as 24 hours. Longer SRTs (>15 days) may increase removal efficiency for some contaminants and allow slower growing bacteria (i.e., nitrifying bacteria) to form, providing a more diverse microorganism community. At the same time, metabolic and co-metabol-

Table 4. Bio-kinetic degradation coefficient (k_{biol}) values for activated sludge in domestic wastewater treatment plants reported in the literature

Pharmaceutical active matter	k_{biol} (L/gSS.day)	SRT (day)	Reference
Naproxen	0.107		
Diclofenac	0.32	5-25	[58]
Ibuprofen	30		
Paracetamol	58-80	10	[45]
Ibuprofen	16 ±2	14-20	[47]
Carbamazepine	0.2	10-12	[57]
Diclofenac	⩽0.5		
Ibuprofen	**17.76**	**10**	**This study**

ic enzymes promoting mineralization of persistent compounds also improves processes [61, 62]. However, the removal efficiencies of some pollutants are independent of SRT. It was stated that some pollutants were absorbed into the sludge in wastewater treatment plants operated with SRT of 10 days [63]. Stasinakis et al. (2010) [64] found the highest biodegradation rates for endocrine disruptors at 3-day low SRT. Gaulke et al. (2009) [65] reported that heterotrophic bacteria capable of degrading pharmaceutical compounds were found at low and high SRTs.

Biodegradation of IBU-2OH and IBU-CBX Metabolites in Batch Activated Sludge System

The change in IBU-2OH and IBU-CBX concentrations according to time is shown in Figure 3. During the biological degradation process, metabolite concentrations gradually decreased over time. The removal efficiency of IBU-CBX from the environment after 5–400 min was higher than the two hydroxylated metabolites. Therefore, IBU-CBX and IBU-2OH are considered to be produced differently with different methods of biodegradation. To clarify these assumptions, IBU-2-OH and IBU-CBX were added separately at 100 µg/L to activated sludge containing 3 g/L biomass, which was identified as the second experiment set. Total removal for all metabolites was achieved after 6 h (Fig. 3). Complete removal of pharmaceutical compounds may depend not only on the biological degradation process but also on the co-effect with the sorption processes. This situation was supported by a study where high concentrations of ibuprofen (43.2–117 ng/g) were found in sludge from wastewater treatment plants [34]. In a study [40], concentrations of ibuprofen and its metabolites were found in river and surface waters changing from 0.7–55.4 ng/L and, another study [66] reported that they could be found in high levels (14.6–31.3 µg/L) in activated sludge systems.

The batch activated sludge system results for the removal of ibuprofen, and its metabolites showed that the removal efficiencies of ibuprofen, IBU-CBX, and IBU-2-OH were about 90%, 27–91%, and 18–82%, respectively.

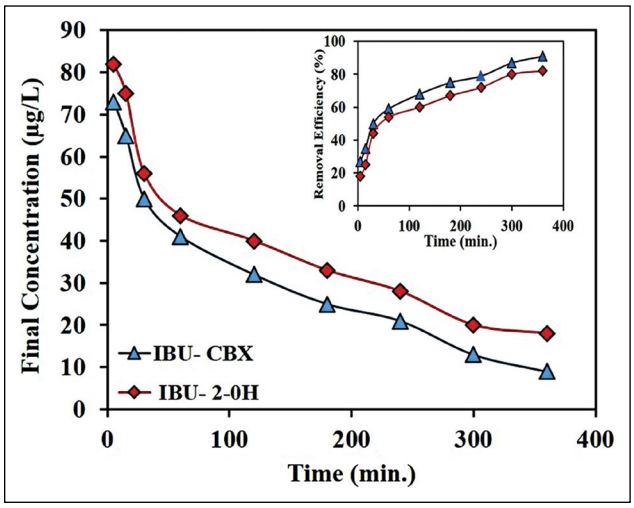


Figure 3. Time variation of 2-OH IBU and IBU-CBX concentrations in experiments performed in batch activated sludge system (100 µg/L metabolite concentration; 3 g/L biomass concentration).

However, it was observed that IBU-2-OH and IBU-CBX are the main metabolites in the biodegradation process of ibuprofen from the data obtained from the studies carried out in the wastewater treatment plant inlet and outlet waters, and this is consistent with the findings obtained in the batch studies conducted in this study. Other studies identified two hydroxy-ibuprofen isomers (IBU-2-OH and IBU-1-OH) as intermediates in ibuprofen mineralization by microorganisms, and they concluded that both intermediates degrade or disappear rapidly in the bioreactor [67]. Metabolites excreted from the body as a result of metabolic activity in humans and the activities of microorganisms in wastewater are the main reasons for the occurrence of these metabolites in wastewater.

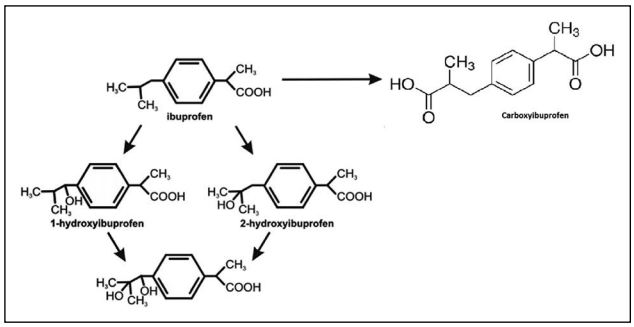


Figure 4. Diagram of possible intermediates formed during the biodegradation of IBU by activated sludge (Figure adapted from [35, 37, 67–69]).

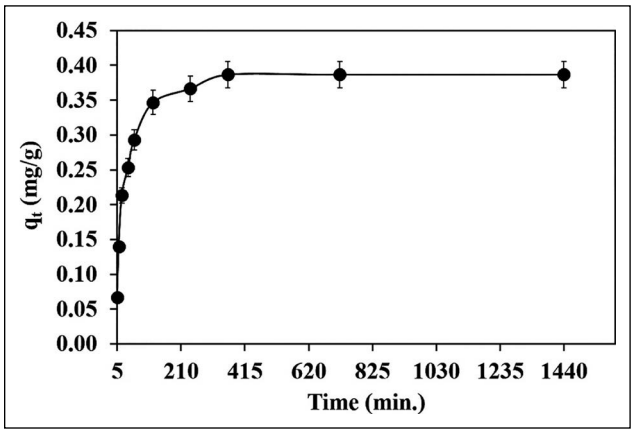


Figure 5. The ibuprofen adsorption over time.

Diagram of possible intermediates formed during the biodegradation of ibuprofen by sludge (Fig. 4). Murdoch and Hay (2015) [67] showed that ibuprofen could convert to carboxylic group by methylation or acetylation of –OH and –COOH group in activated sludge. Many studies have reported that carboxy-ibuprofen (CBX-IBU), 2-hydroxy-ibuprofen (2-OH-IBU) and 1-hydroxy-ibuprofen (1-OH-IBU) compounds can be formed throughout the biodegradation of IBU by activated sludge [31, 40]. The metabolic mechanism consists of hydroxylation, methyl groups oxidation to alcohols, esterification of aldehyde, acidic groups and carboxylic acid after hydroxylation and decarboxylation processes [68].

Adsorption Study

According to the results, approximately 4% of ibuprofen adsorption occurred within the first 20 min and about 6% within 240 min (Fig. 5). At the end of this period, the adsorption rate gradually decreased, and maximum removal efficiency (7.07%) was achieved in 1440 min. It can be said that there is a low affinity between the inactivated sludge and the ibuprofen.

From the plot of the intra-particle diffusion diagram (data not shown), it was observed that the line passing through the $t^{1/2}$ and q_t points did not cross the origin. Singh et al. (1998) [70] stated that this is a sign that the control mechanism is not only pore diffusion. Another explanation was made by Lakshmi et al. (2009) [71]. They reported that this may be due to the mass transfer rate differences between the last and first adsorption periods.

The comparison of the kinetic model coefficients obtained in this study and the literature is given in Table 5. As seen

Table 5. Comparison of kinetic model coefficients in this study and literature for ibuprofen adsorption

Kinetic model	This study	[73]	[74]	[77]
Intraparticle diffusion	C : 0.18 k_{id} : 0.0076 (mg/g $min^{1/2}$) R^2 :0.596	C : 6.221 k_{id} :0.223 (mg/g $min^{1/2}$) R^2 :0.923	k_{id} :9.62 (µg/g $min^{1/2}$) R^2 :0.987	C : 0.008 k_{id} :4.178 (mg/g $min^{1/2}$) R^2 :0.899
Elovich	α : 0.09 (mg/g min) β :16.67 (g/mg) R^2 :0.903	α : 2.975 (mg/g min) β :1.58 (g/mg) R^2 :0.960	α : 25.7 (µg/g min) β :0.055 (µg/g) R^2 :0.999	α : 2.5 (mg/g min) β :3.831 (g/mg) R^2 :0.893
Pseudo-first-order	k_1 : 0.0032 (min-1) q_e : 9.83 (mg/g) R^2 : 0.634	k_1 : 0.00737 (min^{-1}) q_e : 3.207 (mg/g) R^2 : 0.898	k_1 :0.094 (g/mg min) q_e : 55.5 (µg/g) R^2 :0.999	k_1 : 0.011 (min^{-1}) q_e : 4.8 (mg/g) R^2 : 0.891
Pseudo-second-order	k_2 :0.14 (g/mg min) q_e : 0.4 (mg/g) R^2 :0.999	k_2 :0.0464 (g/mg min) q_e : 8.217 (mg/g) R^2 :0.999	k_2 :0.021 (g/mg min) q_e : 55.5 (µg/g) R^2 :0.995	k_2 :0.133 (g/mg min) q_e : 4.804 (µg/g) R^2 :0.999

in Table 5, ibuprofen adsorption best fits the pseudo-second-order model with 0.999 R^2. Based on the fit to the pseudo-second-order kinetic model, it can also be said that adsorption may be dominated by electron sharing or exchange between ibuprofen and dead bacteria [72]. The data obtained are in good agreement with the literature [73, 74]. Streit et al. (2021) [75] used an adsorbent derived from sludge for ibuprofen removal. They reported the pseudo-second-order kinetic model was more suitable for the removal of ibuprofen and the equilibrium time was 180 min. They attributed the adsorption balance in 180 min to the great affinity between ibuprofen and the adsorbent. Correlation coefficients for other kinetic models are examined in Table 5. It appears that ibuprofen adsorption does not fit well the models except for the pseudo-second-order model. From these data, it can be concluded that the adsorption mechanism may be predominantly non-physical, not controlled by the internal surface adsorption and liquid diffusion process. Other studies in the literature [76, 77] have shown that ibuprofen adsorption is more suitable for the pseudo-second-order kinetic model.

When compared the results of biodegradation and adsorption studies under the same initial ibuprofen concentrations (8.2 mg/L), it can be said that removal of ibuprofen with biodegradation (95%) more than abiotic sorption process (7.07%). Moreover, lower removal of ibuprofen was observed in abiotic controls, confirming that the removal is mainly dependent on biological activity. Previous studies showed that ibuprofen is generally removed by biological degradation and adsorption is lower, and volatilization appears negligible, and this is in good agreement with our results [55, 78].

CONCLUSIONS

In this study, using a sensitive analytical method based on the UPLC-QqLiT system, the removal efficiency of ibuprofen, IBU-CBX, and IBU-2-OH metabolites were determined in a batch activated sludge process. Ibuprofen had a removal efficiency of over 90%, while IBU-CBX and IBU-2-OH were removed at efficiencies approximately 27–91% and 18–82%, respectively. The k_{biol} value obtained for ibuprofen was 17.76 L/gSSday. Also, up to 7.07%, ibuprofen removal was observed under the abiotic condition, showing a low affinity between the inactivated sludge and the ibuprofen. The ibuprofen removal best fitted the pseudo-second-order kinetic (R^2=0.99). Per gram inactivated sludge adsorbed 8.217 mg ibuprofen. The ibuprofen can be successfully removed from aqueous environments, and IBU-CBX and IBU-2-OH metabolites can partially remove with an activated sludge process. The findings can contribute to further studies about the removal of ibuprofen transformation products (TP) and TP formation kinetics from aqueous environments.

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DATA AVAILABILITY STATEMENT

The authors confirm that the data that supports the findings of this study are available within the article. Raw data that support the finding of this study are available from the corresponding author, upon reasonable request.

CONFLICT OF INTEREST

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

ETHICS

There are no ethical issues with the publication of this manuscript.

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