International Journal of Environmental Impacts
Vol. 8, No. 2, April, 2025, pp. 311-320
Journal homepage: http://iieta.org/journals/ijei

Performance Evaluation of Wastewater Treatment Plants in Removing Ibuprofen: A Case Study of Babylon Governorate, Iraq

Ali Mohsen Mohammed*, Aalaa Fahim Abbas, Haider Mashkoor Hussein

Department of Ecology, College of Science, University of Qadisiyah, Diwanyiah 58001, Iraq

Corresponding Author Email: alij199011@gmail.com

https://doi.org/10.18280/ijei.080211

Received: 4 November 2024
Revised: 1 February 2025
Accepted: 11 February 2025
Available online: 30 April 2025

Keywords:
high-performance liquid chromatography (HPLC), ibuprofen, wastewater treatment plant (WWTPs), P-value

ABSTRACT

Ibuprofen (IBU) is considered an emergent pollutant owing to its presence in different environmental matrixes (especially in wastewater), high stability, low degradation rate, and widespread use. The purpose of the present investigation was to examine the occurrence of IBU in both the effluent and influent of wastewater treatment plants (WWTPs) and to assess the capacity of these facilities to reduce its concentration. Samples were collected monthly from January to December 2024 from five plants within Babylon Governorate, Iraq: Al-Sadiq Hospital, Marjan Hospital, Al-Hilla Hospital, Childbirth and Children's Hospital, and Mamira plant. The concentration of IBU was conducted utilizing high-performance liquid chromatography (HPLC). The concentration of ibuprofen in the influent wastewater of the plants was 144, 12.57, 10.45, 20.34 and 1096 µg/ l respectively, while revealing effluent concentrations of 132.6, 7.52, 8.05, 11.15 and 945 µg/ l for Al-Sadiq Hospital plant, Marjan Hospital plant, Al-Hilla Hospital plant, Childbirth and Children's Hospital plant, and the Al-Mamira plant respectively. The maximum effluent concentration of IBU was observed at the Mamira plant, exhibiting a removal efficiency of 13.78%, whereas the minimum effluent concentration was recorded at the Childbirth and Children's Hospital plant, which had a removal efficiency of 45.18%. The P-value of 1.025E-06 (less than 0.05) revealed that the influent concentration of ibuprofen exerted a statistically significant impact on the effluent concentration of ibuprofen.

1. INTRODUCTION

The rise in the usage of non-steroidal anti-inflammatory drugs (NSAIDs) has significantly influenced their prevalence in both freshwater sources and wastewater systems. Among these drugs, ibuprofen (IBU) 2-(4-2-Methylpropyl propionic acid) stands out as one of the most common drugs in human and veterinary medication and is listed in the WHO's "Essential Drug List" [1-3]. Its applications encompass the treatment of conditions such as fever, headaches, toothaches, muscle soreness, osteoarthritis, gout, pericarditis, and cancer [4, 5]. The environmental presence of IBU primarily stems from its extensive consumption, inherent molecular stability, inefficient breakdown within the human system, and improper disposal practices involving unused or expired IBU [6, 7].

IBU is more commonly observed as an active compound in the effluent and influent of wastewater treatment facilities. Concentrations of IBU in final effluents and surface water typically fluctuate from 0.018 to 4.24 µg L^{-1} and 0.042 to 1.26 µg L^{-1}, correspondingly [8, 9]. Despite being considered highly biodegradable with removal rates exceeding 90%, metabolites of IBU persist in the effluents of biological wastewater treatment plants (WWTPs) [2]. Humans excrete large amounts of IBU and its metabolites, which are gathered in WWTPs. IBU is not entirely eliminated despite the use of various treatments; because of the high hydrophobicity of the IBU molecule, some of it remains in the effluent treated waters and some of it is adsorbed to sewage sludge. IBU can be used by aquatic or plant life, while WWTP effluents are released into surface waters or applied to land. In addition, IBU and other organic contaminants can infiltrate soils through direct sewage sludge discharge as fertilizers, which can also seep into groundwater as a result of soil irrigation [10].

The substantial lipophilicity of IBU, characterized by a high log K_{ow} value of 3.49, is attributed to the structural 2-methylpropyl group and the absence of additional oxygen moieties. This molecular feature enables IBU to efficiently traverse biological membranes, leading to its wide distribution across living organisms, with a distribution coefficient of 0.18 liters per kilogram [11]. Consequently, IBU demonstrates a propensity for bioaccumulation in marine [12] and freshwater organisms, including mollusks [13], fish [14], mammals [15], and plants [16], further exhibiting biomagnification within food chains [17]. The accumulation of IBU in vertebrates and invertebrates can lead to adverse influences, including DNA damage, oxidative stress, inhibition of specific enzyme functions (such as protein nitration), mitochondrial dysfunction, and lipid peroxidation [18-20]. Recent investigations have revealed IBU's role in promoting the dissemination of antibiotic resistance by facilitating the acquisition of exogenous antibiotic resistance genes. This phenomenon is linked to IBU-induced bacterial competence, oxidative stress, increased production of reactive oxygen species, and enhanced cellular membrane permeability [19, 21].

Rastogi et al. [22] conducted an assessment of the Hazard Quotient (HQ) for diverse aquatic organisms exposed to effluents from WWTPs and riverine water, revealing that IBU exhibited toxicological effects on Vibrio fischeri, Daphnia magna, and various algal species. Furthermore, Richards et al. [23] elucidated a considerable ecotoxicological hazard linked to the presence of IBU in urban wastewater, impacting both algal and fish communities; additionally, Richmond et al. [24] identified toxicological impacts stemming from wastewater emanating from treatment facilities situated in proximity to Hospitals on fish populations, while Xie et al. [13] confirmed the presence of IBU within the tissues of freshwater invertebrates. The bioaccumulation of IBU and its derivatives within vegetative tissues has also been documented, indicating a possibility for transference to various organisms, humans included, despite the observation that their concentrations did not elicit phytotoxic effects [10]. Certainly, humans will be absolutely exposed through the consumption of contaminated aquatic organisms or already-irrigated plants [25]. The excessive consumption of IBU by humans can lead to life-threatening effects, such as mild heart failure, liver failure, kidney problems, renal toxicity, metabolic acidosis, hepatic injury, and severe hypersensitivity reactions, among other health disorders [26-28].

The issue of pharmaceutical pollution, particularly that of IBU, is complex due to the limited availability of effective strategies for capturing, extracting, or removing these compounds in a controlled and efficient manner [29, 30]. The present research sought to quantify the concentration of IBU in the effluent and influent discharged by WWTPs in Babylon Governorate, Iraq. Additionally, the capacity of these WWTPs to remove IBU and achieve minimal effluent concentrations that safeguard human health and the environment was evaluated. Nonetheless, this study offers valuable insights into IBU levels in wastewater, enhancing our understanding of its environmental behavior and hazardous impact on human health and other living beings. The results can be utilized to develop more effective wastewater treatment strategies by incorporating advanced treatment stages.

2. MATERIALS AND METHODES

2.1 Chemicals and reagents

An analytical standard of IBU was acquired from the State Company for Drugs Industry and Medical Appliances (SDI Samara, Iraq) for calibration purposes. HPLC-grade acetonitrile was purchased from Merck in Darmstadt, Germany. Chloroform was supplied by Chemicals BDH Ltd., Poole, England. Analytical-grade formic acid was employed. MF Millipore membrane filters, composed of mixed cellulose esters with a pore size of 0.45 µm, were acquired from Merck, Darmstadt, Germany. Sudan I and Sudan II analytical standards were purchased from Loba Chemie, India. Phosphotungstic acid was obtained from Fisher Scientific. Lead acetate paper was procured from Tedia Co., Fairfield, OH. Stock standard solutions of ibuprofen (100 µg mL^{-1}) were prepared in acetonitrile. Standard working solutions for sample spiking were prepared by diluting the stock solution.

2.2 Sample collection

This study investigated IBU concentrations in five wastewater treatment plants within the Babylon Governorate, Iraq: Al-Sadiq Hospital plant, Marjan Hospital plant, Al-Hilla Hospital plant, Childbirth and Children's Hospital and Mamira plant, the photos of these WWTPs are shown in Figure 1. A total of 72 samples were collected throughout the year of 2024 (January-December), one per month from the effluent and influent sewage of each wastewater treatment plant (WWTP), following the methodology outlined by Richmond et al. [24]. Samples were taken from three different locations before the screen and three locations after the activated sludge tank using clean and sterile glass bottles (2.5 liters), always in the early morning hours. Wastewater samples were subsequently conveyed directly to the research laboratory utilizing an isolated cooler container filled with ice cubes. These samples were stored in brown glass bottles at 4° C in a freezer prior to the extraction process. All samples have been extracted within a timeframe of 48 hours, then filtered via 0.45µm membrane filter before the process of extraction.

Figure 1. Photos of the WWTPs

2.3 Extraction of wastewater samples

Wastewater samples were extracted using a liquid-liquid extraction method based on Ashfaq et al. [31] with minor alterations. In brief, 50 mL of wastewater was mixed with 20 mL of chloroform in three separate extractions (total volume 60 mL) within a separatory funnel. The mixture was agitated for 10 minutes and left to settle and the aqueous and organic layers. The organic layer was collected and then evaporated until dry at a temperature of 38°C. The remaining substance has been re-formed in 2 mL of a solvent mixture containing 85% acetonitrile and 15% acidified water (at pH 3.0) before being transferred to a vial (2 mL) for subsequent chromatographic analysis. The remaining residue was dissolved in 2 mL of a solvent mixture containing 85% acetonitrile and 15% acidified water (pH 3.0) and transferred to a 2 mL vial for subsequent chromatographic examination. The method demonstrated recovery rates ranging from 85% to 95%, ensuring reliable extraction efficiency. The limit of detection (LOD) for IBU was around 0.05 µg L^{-1}, while the limit of quantification (LOQ) was around 0.1 µg L^{-1}, making this method sensitive and effective for trace analysis of IBU in wastewater.

2.4 HPLC analysis

High-Performance Liquid Chromatography (HPLC) is an analytical technique employed for analyzing complex mixtures (as shown in Figure 2). This analysis method starts with sample preparation, where the sample is dissolved in a solvent and filtered. A small volume is then injected into the system. The mobile phase, a liquid solvent or mixture, is pumped under high pressure through a column containing the stationary phase. Components in the sample interact inversely with the mobile and stationary phases, leading to their separation. Separated components pass through a detector, such as UV-Vis or mass spectrometry, which generates a signal. This signal produces a chromatogram with peaks used to identify and quantify the components. Finally, the system is flushed with solvents to remove residues, ensuring consistent performance [32].

An Agilent Series 1100 HPLC system with UV and FLD detectors was used for IBU separation and detection. The system included a degasser, pump, and autosampler. Separation and detection followed [24]. Briefly, Analytes were separated on a Zorbax Eclipse XDB-C18 column (4.6 mm x 150 mm, 5 µm) at ambient temperature. Mobile phase: 60:40 (v/v) acetonitrile/ultrapure water (acidified to pH 3.0 with formic acid). Isocratic elution has been achieved at a flow rate 0.8 mL min^{-1}. The system was programmed with a 3-minute re-equilibration time between consecutive injections and a 20 µL injection volume. UV detection at 230 nm for quantification. fluorescence detection (FLD) utilized excitation and emission wavelengths of 230 nm and 302 nm, respectively, specifically for ibuprofen detection. Both UV and FLD detectors were used simultaneously during each chromatographic run. Fluorescence detection served for ibuprofen (IBU) confirmation by matching its retention times in both UV and FLD chromatograms. Analytes identification relied on comparing retention times in the sample solution to standard solutions. IBU quantification was achieved using matrix-matched calibration curves generated after spiking matrix extracts.

Figure 2. Photos of the HPLC

To ensure the accuracy and reliability of the analytical results, several quality assurance and quality control (QA/QC) procedures have been applied. These included regular calibration of instruments, analysis of blank samples, preparation of standard curves, analysis of duplicate samples, participation in inter-laboratory comparison programs, use of certified reference materials, and detailed record-keeping. These procedures helped to detect and minimize errors, ensure compliance with regulatory standards, and provide confidence in the results.

3. RESULTS AND DISCUSSIONS

The chromatograms of IBU for standard solution and wastewater plants are shown in Figures 3 to 8. The concentrations of IBU were determined using a standard calibration curve. The curve was prepared by analyzing standard solutions of known concentrations using HPLC, and the peak area for each concentration was recorded to establish a linear equation. Then, the concentration of unknown samples was calculated by comparing their peak areas with the standard calibration curve as shown in Table 1.

Table 1. Annual ibuprofen concentration in the effluent and influent of WWTPs

Sample	Influent Concentration (µg/L)	Effluent Concentration (µg/L)	P-value
Al-Sadiq Hospital Plant	144	132.6	
Marjan Hospital Plant	12.57	7.52	
Al-Hilla Hospital Plant	10.45	8.05	1.025E-06
Childbirth and Children's Hospital Plant	20.34	11.15	
Al-Mamira Plant	1096	945	

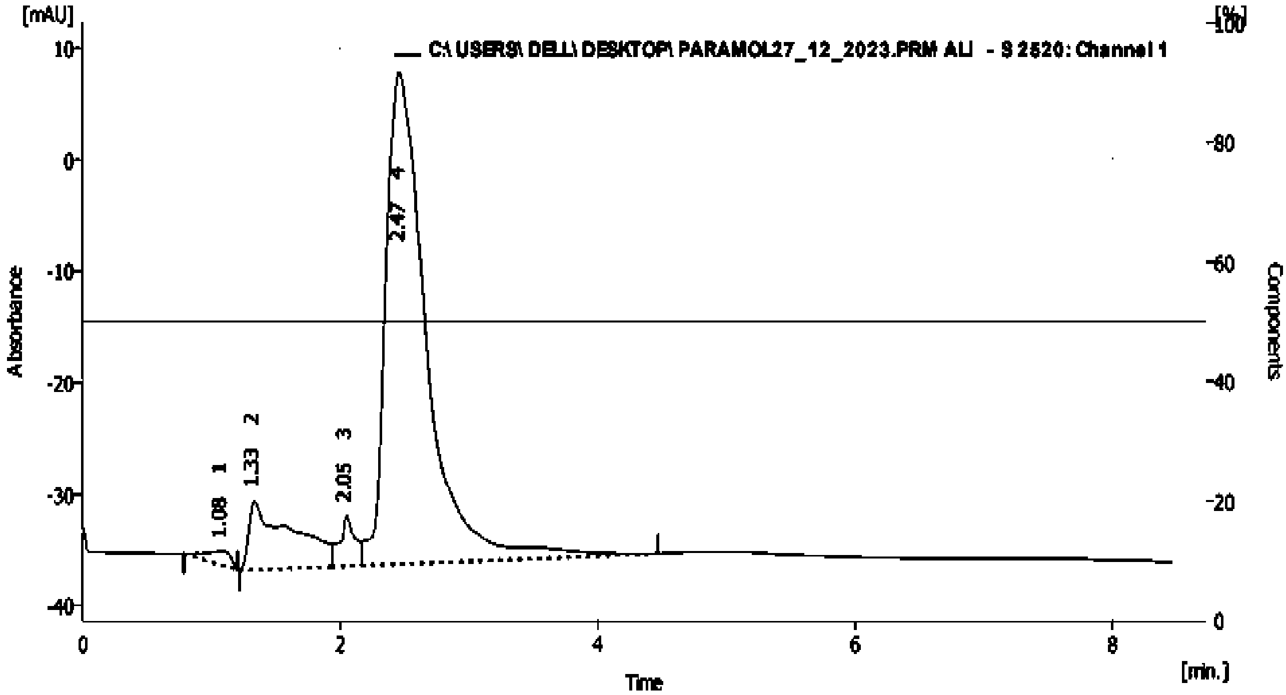

Figure 3. Stander of appliances SDI ibuprofen obtained from the state company for drugs industry and medical samara

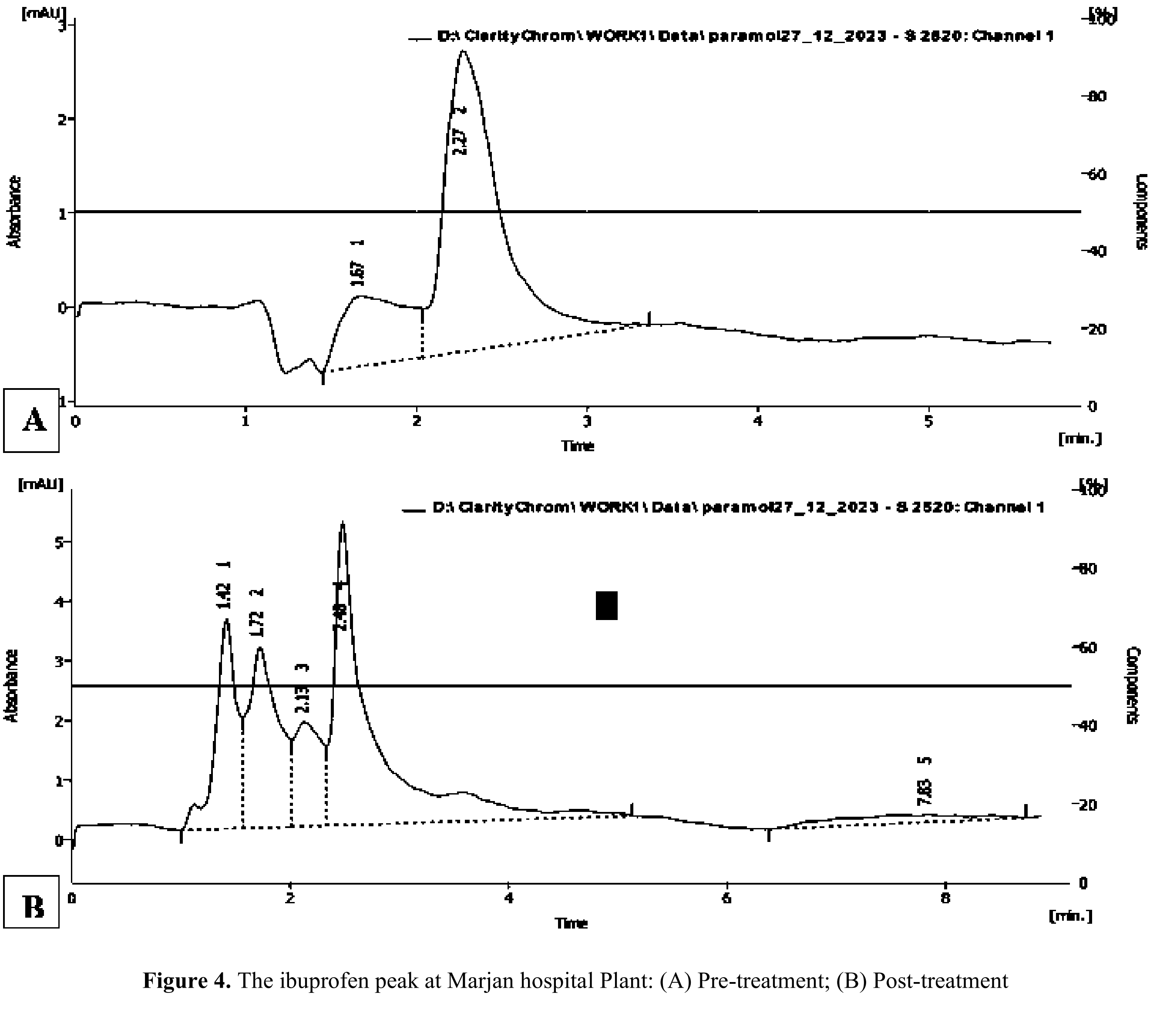

Figure 4. The ibuprofen peak at Marjan hospital Plant: (A) Pre-treatment; (B) Post-treatment

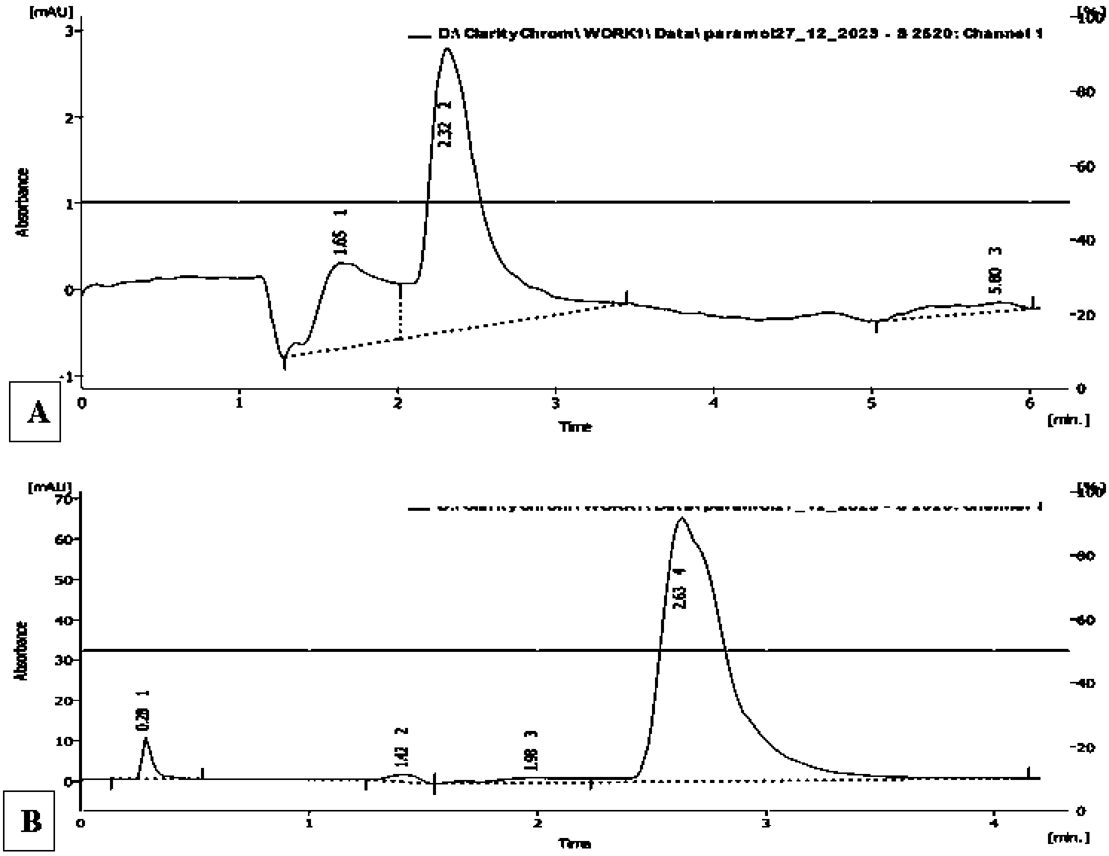

Figure 5. The ibuprofen peak at Al-Hilla hospital plant: (A) Pre-treatment; (B) Post-treatment

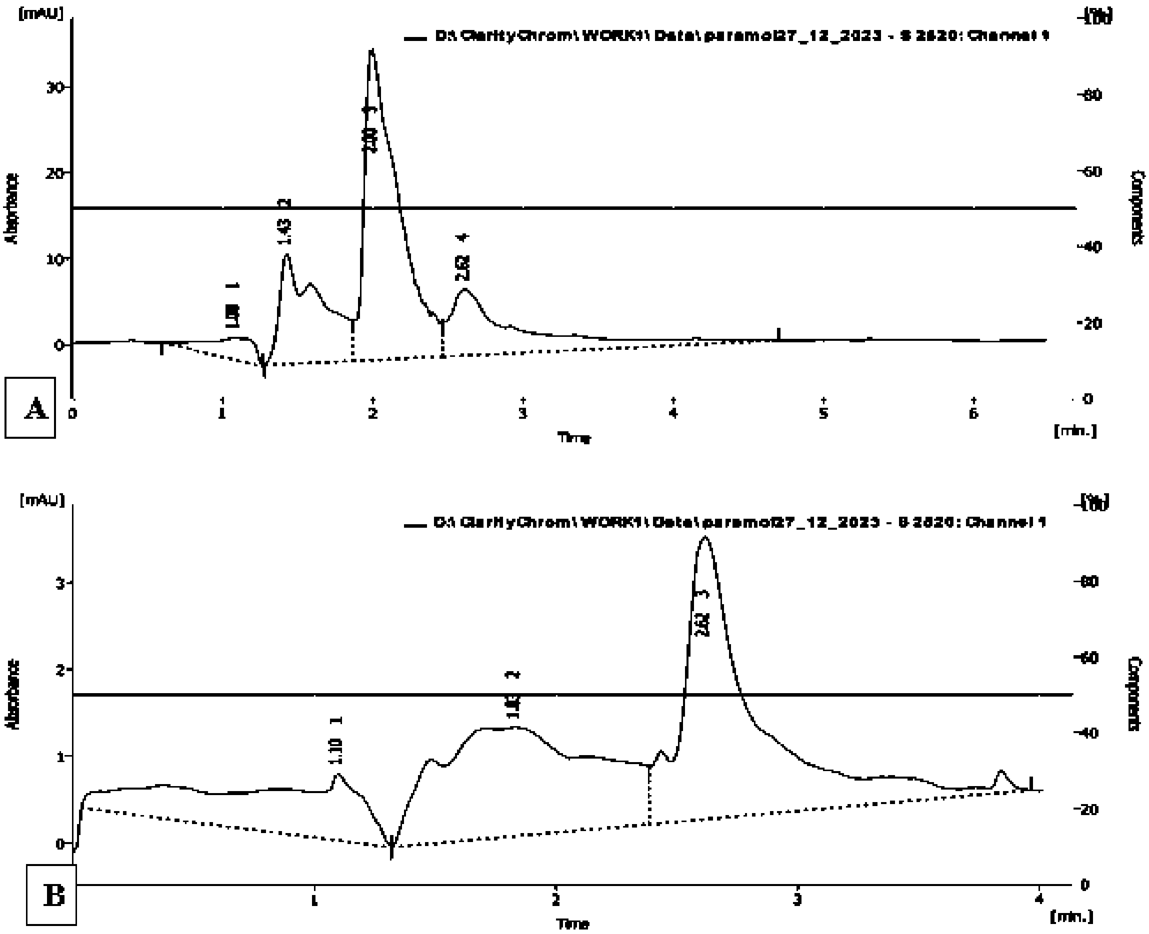

Figure 6. The ibuprofen peak at Al-Sadiq hospital plant: (A) Pre-treatment; (B) Post-treatment

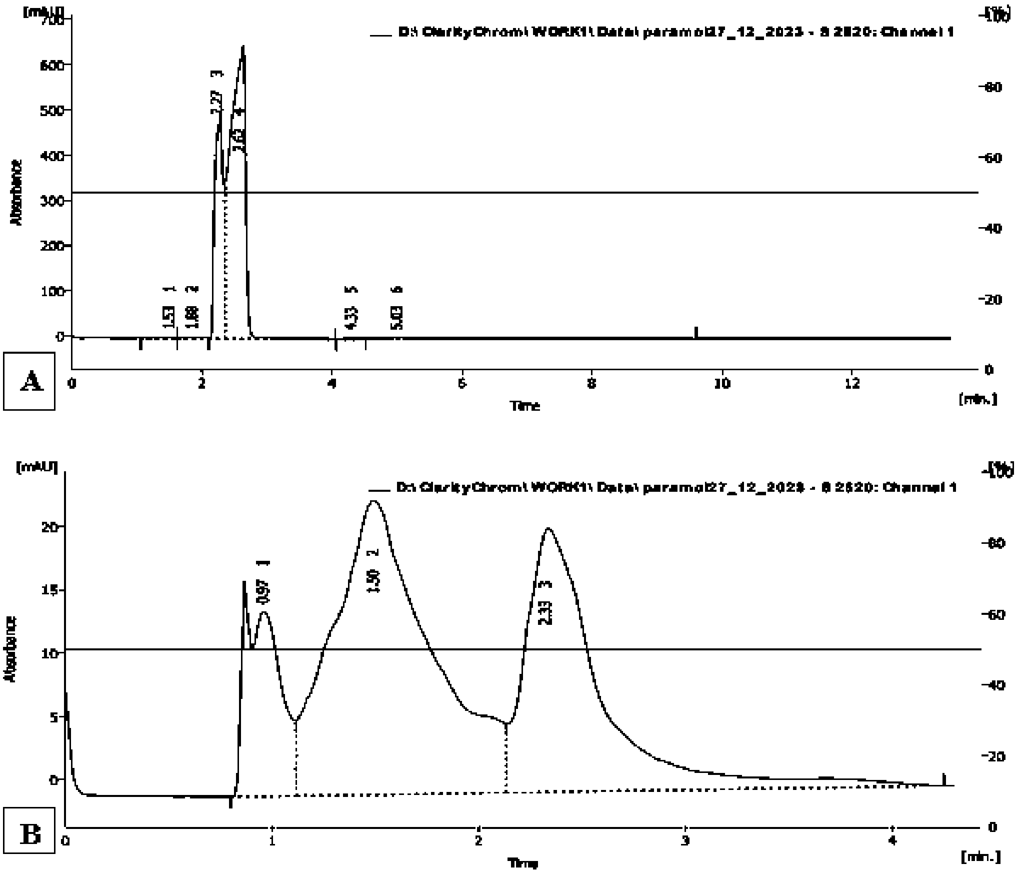

Figure 7. The ibuprofen peak at Al-Mamira plant: (A) Pre-treatment; (B) Post-treatment

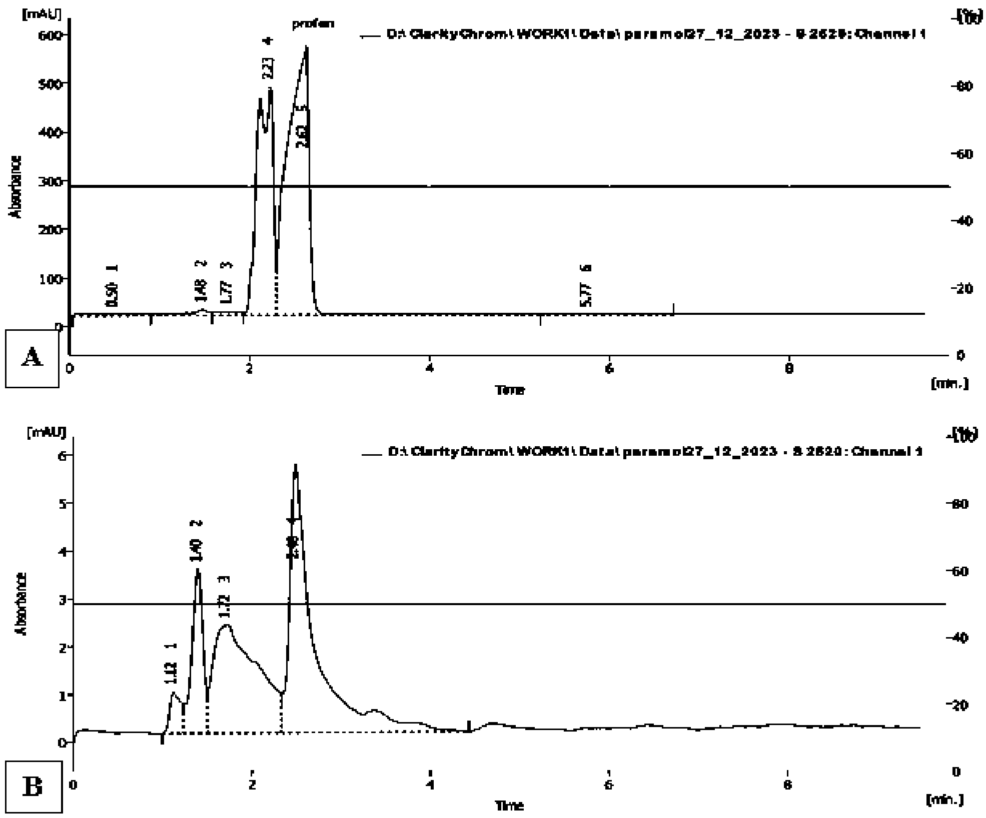

Figure 8. The ibuprofen peak at childbirth and children's hospital plant: (A) Pre-treatment; (B) Post-treatment

Generally, the wastewater treatment plant in the targeted sites employed both physical and biological methodologies, specifically utilizing activated sludge aeration. The preliminary treatment phase initiates with a bar screen, facilitating the removal of solid particulates, succeeded by the extraction of grits. The primary treatment encompasses a sedimentation basin, which may incorporate optional physical and chemical interventions, along with equalization/homogenization tanks. The secondary biological treatment is executed through an activated sludge mechanism utilizing conventional aeration techniques in aerated tanks, supplemented by secondary sedimentation coupled with the recirculation of biological sludge. The quantification of ibuprofen was conducted on influent and effluent samples sourced from wastewater treatment facilities. IBU was detected in all sewage samples analyzed. Table 1 presents the results derived from this investigation.

In this study, the influent concentration of IBU exhibited a notable elevation at the Al-Mamira plant, quantified at 1096 µg/L, followed by Al-Sadiq Hospital plant with a concentration of 144 µg/L, Childbirth and Children's Hospital plant with 20.34 µg/ L, Marjan Hospital plant with 12.57 µg/L, and finally Al-Hilla Hospital plant at 10.45 µg/L. However, the maximum effluent concentration of wastewater of IBU was 945 µg/L in Al-Mamira plant, followed by Al-Sadiq Hospital plant with concentration of 132.6 µg/L, then Childbirth and Children's Hospital plant with 11.15 µg/L, and Al-Hilla Hospital plant with 8.05 µg/L, whereas the minimum effluent concentration was 7.52 µg/L in Marjan Hospital Plant. It is worth noting that the influent and effluent IBU concentrations in the Al-Mamira plant were significantly higher compared to the other plants. This is attributed to the fact that it is the main plant receiving wastewater from the entire governorate of Babylon, including domestic, medical, and commercial sources.

The P-value was selected by regression test, using SPSS software (V.28 Inc., Chicago, USA). From the previous table, we found that the p-value of 1.025E-06 less than 0.05, which signified that there was a statistically significant relationship between the two variables, suggesting that the influent concentration of IBU had a considerable influence on the effluent concentration of IBU. The extremely low p-value indicates that the probability of obtaining these results by chance was negligible, thereby reinforcing our confidence in the existence of a real relationship between influent and effluent IBU concentrations. This implies that the treatment technologies employed in these plants significantly influence the removal of IBU from wastewater.

According to current results (Table 2), the removal efficiency of Childbirth and Children's Hospital plant was higher than the other investigated wastewater plants with rate of 45.18 %, followed by Marjan Hospital plant with 40.13%, Al-Hilla Hospital plant with 22.97 %, and Al-Mamira plant with 13.78 %, while the minimum removal efficiency of 7.92 % was in Al-Sadiq Hospital plant. The percentage removal equation of IBU concentration was calculated as follows [33]:

$$\text{Percentage removal \%} = \frac{\text{Co} - \text{Ce}}{\text{Co}}$$

where,

C_o = Influent concentration of IBU, µg/L.

C_e = Effluent concentration of IBU, µg/L.

Table 2. Percentage removal of IBU in WWTPs, %

No.	Name of Plant	Percentage Removal (%)
1	Al-Sadiq Hospital Plant	7.92
2	Marjan Hospital Plant	40.18
3	Al-Hilla Hospital Plant	22.97
4	Childbirth and Children's Hospital Plant	45.18
5	Al-Mamira Plant	13.78

IBU is not effectively eliminated by conventional wastewater treatment plants strategies. Furthermore, IBU is problematic to break down in the primary treatment units or by means of microorganisms in activated sludge reactor due to their persistence and physicochemical properties (high lipophilic degree, low water solubility and low biodegradation). The physicochemical properties of IBU significantly hinder its removal by conventional wastewater treatment processes. This result consisted with [4, 34-39].

Secondary treatment involving biological processes has the potential to be more resilient for the elimination of organic substance by microorganisms present in activated sludge reactors, utilizing it as an energy and carbon source within their metabolic processes. These micro-organisms are not effective against IBU in facilitating the degradation of IBU due to its chemical stability, and resistance to biodegradation [40, 41]. Additionally, insufficient hydraulic retention time in treatment tanks and suboptimal environmental conditions, including temperature, pH, and dissolved oxygen levels, can hinder the activity of microorganisms responsible for IBU degradation [42, 43]. Consequently, it is suggested that the biodegradation of IBU is contingent upon the capabilities of microorganisms to synthesize specific enzymes requisite for IBU degradation [5]. Also, the degradation of IBU has revealed that elevated concentrations of IBU exert an inhibitory influence on microbial populations [44]. However, IBU was not adequately eliminated in the presently functioning biological wastewater treatment systems characterized by elevated organic loading, which primarily concentrate on the decrease of chemical oxygen demand and the removal of nutrients [34, 35].

It is noteworthy that seasonal variations in IBU concentrations in wastewater significantly influenced the assessment of IBU levels in this study. IBU concentrations in wastewater increased during the winter season due to higher consumption rates associated with increased cold and flu cases. Additionally, lower temperatures in winter slowed down the degradation rate of IBU in the biological treatment system, as they inhibited the activity of microorganisms responsible for degradation. Moreover, reduced water usage during this season led to a decrease in wastewater volume, resulting in relatively higher IBU concentrations. To address these challenges, frequent sampling of wastewater from the mentioned treatment plants was conducted throughout the year to determine IBU concentrations.

4. CONCLUSION

The IBU concentration levels detected within the effluent were notably elevated, suggesting a diminished efficacy of WWTPs in the removal of IBU and highlighting the inadequacies of contemporary sewage treatment systems in fully eradicating this pollutant. In this study, the influent IBU concentration was highest at the Al-Mamira plant (1096 μg/L), followed by Al-Sadiq Hospital (144 μg/L), Childbirth and Children's Hospital (20.34 μg/L), Marjan Hospital (12.57 μg/L), and Al-Hilla Hospital (10.45 μg/L). In contrast, the effluent IBU concentration was highest at the Al-Mamira plant (945 μg/L), followed by Al-Sadiq Hospital (132.6 μg/L), Childbirth and Children's Hospital (11.15 μg/L), and Al-Hilla Hospital (8.05 μg/L). The lowest effluent concentration was found at Marjan Hospital (7.52 μg/L). It is worth noting that the highest IBU quantities were discovered in the effluent and influent wastewater of the Al-Mamira plant, reaching 945 and 1096 μg/L, respectively. In contrast, the lowest effluent concentration was observed at the Marjan Hospital plant (7.52 μg/L), and the lowest influent concentration was found at the Al-Hilla Hospital plant (10.45 μg/L). Accordingly, the removal efficiency of Childbirth and Children's Hospital plant was higher than the other investigated wastewater plants with rate of 45.18 %, followed by Marjan Hospital plant with 40.13%, Al-Hilla Hospital plant with 22.97 %, and Al-Mamira plant with 13.78 %, while the minimum removal efficiency of 7.92 % was in Al-Sadiq Hospital plant. It is imperative that further improvements and modifications be undertaken to achieve the comprehensive removal of this compound, thereby mitigating potential risks to public health. The measures taken to address this issue include the introduction of specific microorganisms capable of degrading IBU, along with providing optimal conditions for their growth, such as improving aeration in treatment tanks, regulating temperature and pH, and increasing retention time. Additionally, incorporating advanced treatment stages like advanced oxidation processes (AOPs), adsorption, coagulation-flocculation, UV/H2O2, membrane filtration, O3/UV, Bioremediation, among others.

REFERENCES

[1] Aguilar-Romero, I., Madrid, F., Villaverde, J., Morillo, E. (2024). Ibuprofen-enhanced biodegradation in solution and sewage sludge by a mineralizing microbial consortium. Shift in associated bacterial communities. Journal of Hazardous Materials, 464: 132970. https://doi.org/10.1016/j.jhazmat.2023.132970

[2] Bashaar, M., Thawani, V., Hassali, M.A., Saleem, F. (2017). Disposal practices of unused and expired pharmaceuticals among general public in Kabul. BMC Public Health, 17: 45. https://doi.org/10.1186/s12889-16-3975-z

[3] Chopra, S., Kumar, D. (2020). Ibuprofen as an emerging organic contaminant in environment, distribution and remediation. Heliyon, 6(6): e04087. https://doi.org/10.1016/j.heliyon.2020.e04087

[4] Czyrski, A. (2019). Determination of the lipophilicity of ibuprofen, naproxen, ketoprofen, and flurbiprofen with thin-layer chromatography. Journal of Chemistry, 2019: 3407091. https://doi.org/10.1155/2019/3407091

[5] Jan-Roblero, J., Cruz-Maya, J.A. (2023). Ibuprofen: toxicology and biodegradation of an emerging contaminant. Molecules, 28(5): 2097. https://doi.org/10.3390/molecules28052097

[6] Marchlewicz, A., Guzik, U., Smułek, W., Wojcieszyńska, D. (2017). Exploring the degradation of ibuprofen by Bacillus thuringiensis B1 (2015b): The new pathway and factors affecting degradation. Molecules, 22(10): 1676. https://doi.org/10.3390/molecules22101676

[7] Mezzelani, M., Gorbi, S., Regoli, F. (2018). Pharmaceuticals in the aquatic environments: evidence of emerged threat and future challenges for marine organisms. Marine Environmental Research, 140: 41-60. https://doi.org/10.1016/j.marenvres.2018.05.001

[8] Murdoch, R.W., Hay, A.G. (2015). The biotransformation of ibuprofen to trihydroxyibuprofen in activated sludge and by Variovorax Ibu-1. Biodegradation, 26: 105-113. https://doi.org/10.1007/s10532-015-9719-4

[9] Parolini, M. (2020). Toxicity of the Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) acetylsalicylic acid, paracetamol, diclofenac, ibuprofen and naproxen towards freshwater invertebrates: A review. Science of the Total Environment, 740: 140043. https://doi.org/10.1016/j.scitotenv.2020.140043

[10] Qu, H., Barrett, H., Wang, B., Han, J., Wang, F., Gong, W., Wu, J., Wang, W., Yu, G. (2021). Co-occurrence of antiseptic triclocarban and chiral anti-inflammatory ibuprofen in environment: Association between biological effect in sediment and risk to human health. Journal of Hazardous Materials, 407: 124871. https://doi.org/10.1016/j.jhazmat.2020.124871

[11] Sadutto, D., Andreu, V., Ilo, T., Akkanen, J., Picó, Y. (2021). Pharmaceuticals and personal care products in a Mediterranean coastal wetland: Impact of anthropogenic and spatial factors and environmental risk assessment. Environmental Pollution, 271: 116353. https://doi.org/10.1016/j.envpol.2020.116353

[12] Wang, Y., Lu, J., Engelstädter, J., Zhang, S., Ding, P., Mao, L., Yang, S., Wang, Z., Pang, S., Yao, J., Han, X., Guo, J. (2020). Non-antibiotic pharmaceuticals enhance the transmission of exogenous antibiotic resistance genes through bacterial transformation. The ISME Journal, 14(8): 2179-2196. https://doi.org/10.1038/s41396-021-01074-x

[13] Xie, H., Hao, H., Xu, N., Liang, X., Gao, D., Xu, Y., Gao, Y., Tao, H., Wong, M. (2019). Pharmaceuticals and personal care products in water, sediments, aquatic organisms, and fish feeds in the Pearl River Delta: Occurrence, distribution, potential sources, and health risk assessment. Science of the Total Environment, 659: 230-239. https://doi.org/10.1016/j.scitotenv.2018.12.222

[14] Xu, B., Xue, G., Yang, X. (2018). Isolation and application of an ibuprofen-degrading bacterium to a biological aerated filter for the treatment of micro-polluted water. Frontiers of Environmental Science & Engineering, 12: 15. https://doi.org/10.1007/s11783-18-1080-5

[15] Ajibola, A.S., Adebiyi, A.O., Nwaeke, D.O., Ajibola, F.O., Adewuyi, G.O. (2021). Analysis, occurrence and ecological risk assessment of diclofenac and ibuprofen residues in wastewater from three wastewater treatment plants in south-western Nigeria. Journal of Applied Sciences and Environmental Management, 25(3): 330-340. https://doi.org/10.4314/jasem.v25i3.5

[16] Ivshina, I.B., Tyumina, E.A., Bazhutin, G.A., Vikhareva, E.V. (2021). Response of Rhodococcus cerastii IEGM 1278 to toxic effects of ibuprofen. PloS One, 16(11): e0260032. https://doi.org/10.1371/journal.pone.0260032

[17] Khalil, A.M., Memon, F.A., Tabish, T.A., Salmon, D., Zhang, S., Butler, D. (2020). Nanostructured porous graphene for efficient removal of emerging contaminants

(pharmaceuticals) from water. Chemical Engineering Journal, 398: 125440. https://doi.org/10.1016/j.cej.2020.125440

[18] Mathias, F.T., Fockink, D.H., Disner, G.R., Prodocimo, V., Ribas, J.L.C., Ramos, L.P., Cestari, M.M., de Assis, H.C.S. (2018). Effects of low concentrations of ibuprofen on freshwater fish Rhamdia quelen. Environmental Toxicology and Pharmacology, 59: 105-113. https://doi.org/10.1016/j.etap.2018.03.008

[19] Pi, N., Ng, J.Z., Kelly, B.C. (2017). Bioaccumulation of pharmaceutically active compounds and endocrine disrupting chemicals in aquatic macrophytes: Results of hydroponic experiments with Echinodorus horemanii and Eichhornia crassipes. Science of the Total Environment, 601: 812-820. https://doi.org/10.1016/j.scitotenv.2017.05.137

[20] Praveenkumarreddy, Y., Vimalkumar, K., Ramaswamy, B.R., Kumar, V., Singhal, R.K., Basu, H., Goswami, R., Kumar, M. (2021). Assessment of non-steroidal anti-inflammatory drugs from selected wastewater treatment plants of Southwestern India. Emerging Contaminants, 7: 43-51. https://doi.org/10.1016/j.emcon.2021.01.001

[21] Ramezani, M., Rad, F.A., Ghahari, S., Ghahari, S., Ramezani, M. (2021). Nano-bioremediation application for environment contamination by microorganism. Microbial Rejuvenation of Polluted Environment: Volume 2, 349-378. https://doi.org/10.1007/978-981-15-7455-9_14

[22] Rastogi, A., Chaudhary, S., Tiwari, M.K., Ghangrekar, M.M. (2024). Ibuprofen degradation by mixed bacterial consortia: Metabolic pathway and microbial community analysis. Chemosphere, 359: 142354. https://doi.org/10.1016/j.chemosphere.2024.142354

[23] Richards, N.L., Cook, G., Simpson, V., Hall, S., Harrison, N., Scott, K.S. (2011). Qualitative detection of the NSAIDs diclofenac and ibuprofen in the hair of Eurasian otters (Lutra lutra) occupying UK waterways with GC–MS. European Journal of Wildlife Research, 57: 1107-1114. https://doi.org/10.1007/s10344-011-0513-2

[24] Richmond, E.K., Rosi, E.J., Walters, D.M., Fick, J., Hamilton, S.K., Brodin, T., Sundelin, A., Grace, M.R. (2018). A diverse suite of pharmaceuticals contaminates stream and riparian food webs. Nature Communications, 9(1): 4491. https://doi.org/10.1038/s41467-018-06822-w

[25] Sánchez-Aceves, L., Pérez-Alvarez, I., Gómez-Oliván, L.M., Islas-Flores, H., Barceló, D. (2021). Long-term exposure to environmentally relevant concentrations of ibuprofen and aluminum alters oxidative stress status on Danio rerio. Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology, 248: 109071. https://doi.org/10.1016/j.cbpc.2021.109071

[26] Singh, A., Pal, D.B., Mohammad, A., Alhazmi, A., Haque, S., Yoon, T., Singh, A.P., Gupta, V.K. (2022). Biological remediation technologies for dyes and heavy metals in wastewater treatment: New insight. Bioresource Technology, 343: 126154. https://doi.org/10.1016/j.biortech.2021.126154

[27] Thalla, A.K. Vannarath, A.S. (2020). Occurrence and environmental risks of nonsteroidal anti-inflammatory drugs in urban wastewater in the southwest monsoon region of India. Environmental Monitoring and Assessment, 192: 193. https://doi.org/10.1007/s10661-020-8161-1

[28] Volans, G. (2015). Human toxicity of ibuprofen. Ibuprofen: Discovery, Development and Therapeutics, 498-517. https://doi.org/10.1002/9781118743614.ch12

[29] Wang, P., Bu, L., Wu, Y., Ma, W., Zhu, S., Zhou, S. (2021). Mechanistic insight into the degradation of ibuprofen in UV/H_2O_2 process via a combined experimental and DFT study. Chemosphere, 267: 128883. https://doi.org/10.1016/j.chemosphere.2020.128883

[30] Żur, J., Piński, A., Marchlewicz, A., Hupert-Kocurek, K., Wojcieszyńska, D., Guzik, U. (2018). Organic micropollutants paracetamol and ibuprofen—Toxicity, biodegradation, and genetic background of their utilization by bacteria. Environmental Science and Pollution Research, 25: 21498-21524. https:// doi.org/10.1007/s11356-018-2517-x

[31] Ashfaq, M., Noor, N., Saif-Ur-Rehman, M., Sun, Q., Mustafa, G., Faizan Nazar, M., Yu, C.P. (2017). Determination of commonly used pharmaceuticals in hospital waste of Pakistan and evaluation of their ecological risk assessment. CLEAN – Soil, Air, Water, 45(6): 1500392. https://doi.org/10.1002/clen.201500392

[32] Belanger, J.M., Paré, J.J., Sigouin, M. (1997). High Performance Liquid Chromatography (HPLC): Principles and applications. Techniques and Instrumentation in Analytical Chemistry, 18: 37-59. https://doi.org/10.1016/S0167-9244(97)80011-X

[33] Al-Khafaji, S.A., Al-Rekabi, W.S. (2021). Evaluation of the hospital's wastewater treatment plant in Basrah province. Journal of Physics: Conference Series, 1973(1): 012033. https:// doi.org/10.1088/1742-6596/1973/1/012033

[34] Novakovic, M., Mihajlovic, I. (2023). A review on conventional and advanced water treatments in ibuprofen removal. Journal of Ecology & Natural Resources, 7(3): 1-8. https://doi.org/10.23880/jenr-16000343

[35] Brillas, E. (2022). A critical review on ibuprofen removal from synthetic waters, natural waters, and real wastewaters by advanced oxidation processes. Chemosphere, 286: 131849. https://doi.org/10.1016/j.chemosphere.2021.131849

[36] Odabasi, S.U. (2021). Ibuprofenin ileri oksidasyon prosesleri ile gideriminin yaşam döngüsü değerlendirmesi. Avrupa Bilim ve Teknoloji Dergisi, (28): 795-801. https://doi.org/10.31590/ejosat.1011436

[37] Sharma, K., Kaushik, G., Thotakura, N., Raza, K., Sharma, N., Nimesh, S. (2019). Fate of ibuprofen under optimized batch biodegradation experiments using Micrococcus yunnanensis isolated from pharmaceutical sludge. International Journal of Environmental Science and Technology, 16: 8315-8328. https://doi.org/10.1007/s13762-019-02400-9

[38] Ferreira, A.P. (2014). Identification and quantification of ibuprofen in conventional wastewater treatment plants in Rio de Janeiro, Brazil, and their discharge to the aquatic environment. Journal of Advances in Biology, 4(1): 305-313. https://is.gd/oUxOYM.

[39] Mezzelani, M., Gorbi, S., Fattorini, D., d'Errico, G., Consolandi, G., Milan, M., Regoli, F. (2018). Long-term exposure of Mytilus galloprovincialis to diclofenac, ibuprofen and ketoprofen: Insights into bioavailability, biomarkers and transcriptomic changes. Chemosphere, 198: 238-248. https://doi.org/10.1016/j.chemosphere.2018.01.148

[40] Jia, Y., Khanal, S. K., Yin, L., Sun, L., Lu, H. (2021). Influence of ibuprofen and its biotransformation products

on different biological sludge systems and ecosystem. Environment International, 146: 106265. https://doi.org/10.1016/j.envint.2020.106265

[41] Yao, M., Duan, L., Song, Y., Hermanowicz, S. W. (2021). Degradation mechanism of ibuprofen via a forward osmosis membrane bioreactor. Bioresource Technology, 321: 124448. https://doi.org/10.1016/j.biortech.2020.124448

[42] Falahi, O.A.A., Abdullah, S.R.S., Hasan, H.A., Othman, A.R., Ewadh, H.M., Al-Baldawi, I.A., Kurniawan, S.B. (2022). Elimination of mixed ibuprofen and paracetamol from spiked domestic wastewater via a pilot continuous aerated sub-surface constructed wetland system. Journal of Water Process Engineering, 50: 103308. https://doi.org/10.1016/j.jwpe.2022.103308

[43] Lara‐Moreno, A., Costa, M.C., Vargas‐Villagomez, A., Carlier, J.D. (2024). New bacterial strains for ibuprofen biodegradation: Drug removal, transformation, and potential catabolic genes. Environmental Microbiology Reports, 16(4): e13320. https://doi.org/10.1111/1758-2229.13320

[44] Wu, J., Zhang, Y., Zhou, Y. (2024). Multi-strategy study of environmental degradation of ibuprofen: From chemical catalysis to biological treatment. E3S Web of Conferences, 53: 3012. https://doi.org/10.1051/e3sconf/202455303012