

Research Article

Fate and Occurrence of Pharmaceutically Active Organic Compounds during Typical Pharmaceutical Wastewater Treatment

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The chemical composition, distribution, and fate of pharmaceutically active compounds (PhACs) present in typical pharmaceutical wastewater treatment plants were investigated with the aim of effectively removing these pollutants while minimizing waste of resources and energy. The results of this study indicate that the relative content of an organic compound class is unrelated to the number of organic compounds in the influent and effluent, yet it is directly proportional to the pollution contribution in pharmaceutical wastewater. In wastewater influent, the organic compound classes with the highest relative contents and pollution contributions were acids (relative content = 63.65%, contribution to pollution = 67.22%), esters (44.96%, 41.24%), and heterocyclic compounds (30.24%, 35.23%); in wastewater effluent, these classes were organic acids (62.54%, 65.13%), esters (52.66%, 59.02%), and organosilicon compounds (42.46%, 37.45%). The different physicochemical characteristics of these pollutants result in different removal efficiencies. For example, *N,N*-dimethylformamide, 4-methyloctane, *N*-ethylmorpholine, and 4-amino-*N,N*- and *N,N*-diethylbenzamide are refractory and are not degraded by microorganisms; thus, these compounds are discharged into the aquatic environment. Other organic compound classes including organosilicon compounds, acids, esters, heterocycles, and alcohols are mostly biodegraded, which leads to high concentrations of hydrocarbons in the wastewater effluent. The results of this study provide a foundation for the improvement of pharmaceutical wastewater treatment.

1. Introduction

The use of pharmaceutically active compounds (PhACs) has greatly increased in recent years. Canadian sales of prescription drugs grew by nearly US\$8 billion between 2006 and 2011 [1], and approximately 1.9 million tons of PhACs were consumed in China in 2009 alone [2]. The manufacture of PhACs involves several waste-producing processes, such as refinement and separation, and the

increase in sales and manufacturing has led to an increase in the discharge of pharmaceutical wastewater [3]. Wastewater treatment plants (WWTPs) are unable to completely remove or transform all PhACs and PhAC metabolites during the treatment process and untreated PhACs are returned to the environment [4]. For some recalcitrant PhACs, such as carbamazepine, diclofenac, and metoprolol, concentrations may be higher in effluent than in untreated influent [5,6].

The potential negative effects of PhACs on aquatic ecosystems, terrestrial ecosystems, and wildlife have initiated research interest in the presence of PhACs in the environment [7–9]. Some toxic organics accumulate in organisms and may reach toxic concentrations through bioaccumulation in the food chain, causing long-term or cumulative toxicity to organisms and the environment [10]. Residual refractory organic compounds in treated pharmaceutical wastewater can also affect human health; for example, antibiotics can induce microbial aberrations, even at low concentrations [11].

Currently, effluent from WWTPs is regarded as one of the major pathways by which PhACs enter aquatic environments such as surface water, groundwater, and river water [6,12]. The existing biotechnology-based pharmaceutical wastewater treatment processes struggle to effectively deal with pharmaceutical contaminants, which has resulted in effluent with high concentrations of refractory organics being discharged into the aquatic environment. With stringent legislative requirements for wastewater treatment and increasingly stringent effluent discharge limits, conventional pharmaceutical wastewater treatment processes are increasingly struggling to meet the standards that are required for effective environmental protection.

To ensure that pharmaceutical wastewater effluent meets the required standards for pollutant concentrations, an advanced treatment technology involving advanced oxidation, membrane filtration, activated carbon adsorption, wet oxidation, etc., has been used to treat refractory organics present in the effluent. However, these advanced treatment technologies usually degrade the PhACs using a nonspecific strategy because the composition, distribution, and fate of PhACs during wastewater treatment are not currently understood. For example, advanced oxidation techniques such as the electro-Fenton process [13] and ozone oxidation [14] produce a strong oxidant, the hydroxyl radical ($\cdot\text{OH}$), which nonspecifically mineralizes PhACs [15, 16]. Despite effectively removing PhACs, nonspecific degradation considerably increases the operating costs of WWTPs because it consumes large quantities of chemicals and energy [17, 18], which is contrary to the goals of environmental sustainability. Therefore, a goal-oriented and classified treatment strategy is needed in order to minimize the resources and energy used by pharmaceutical wastewater treatment and achieve environmental sustainability while effectively removing pollutants. A key step towards this goal is to effectively identify the chemical composition, distribution, and fate of high concentration refractory organics in effluent and to establish the fingerprint of PhACs from typical pharmaceutical wastewater effluent.

Currently, most studies have focused on determining the concentration of PhACs in the aqueous phase and calculating their overall removal efficiencies based on the concentrations of PhACs in raw influent and final effluent. Few studies have considered the distribution of PhACs in individual treatment processes, such as primary treatment, biological treatment, and chlorination. This study investigated four aspects of PhAC treatment in WWTPs: the organic compound classes and distribution of PhACs in the influent and effluent of three typical pharmaceutical wastewater treatment plants; the

occurrence and fate of organic compounds during different stages of a conventional treatment process that employs “primary treatment + anaerobic + aerobic + sedimentation”; the relationship between chemical oxygen demand (COD) and theoretical oxygen demand (ThOD); and the major pollutants remaining in the final effluent, as determined by contributions to COD. The results of this study provide a foundation for the improvement of pharmaceutical wastewater treatment.

2. Materials and Methods

2.1. Sample Collection. In this study, six sampling sites were chosen within three different types of typical pharmaceutical treatment plants throughout the city of Chongqing, namely, antibiotic wastewater treatment plant, Chinese traditional medicine wastewater treatment plant, and chemical synthesis wastewater treatment plant. We collected water samples from the influent and effluent at June in 2017 (sample was collected every other week for a total of three samples from each location). As shown in Figure 1, A, C, and E represent influent sampling sites and B, D, and F represent effluent sampling sites. Five additional sampling sites were chosen at the pharmaceutical factory with a typical traditional treatment process of “primary treatment + anaerobic + aerobic + sedimentation.” G, H, I, J, and K represent the sampling sites in the typical traditional treatment process.

Collected water samples were placed in clean, 1 L amber glass bottles. A water grab sampler was used to collect water at each site. The water sample was mixed for 24 h, the sampling frequency was 1 L/h, and the total volume was 24 L. Each bottle was prerinsed with Milli-Q water in the laboratory and then rinsed twice with the sample water prior to sample collection. NaN_3 (0.5 g/L) or hydrochloric acid was added to inhibit microbial activity. Three parallel samples were collected, and one sample of these samples was used to determine measurement parameters. All samples were transferred to the laboratory for analysis, stored at 4°C, and analyzed within 24 h.

2.2. Sample Preparation. Prior to analyzing a sample, the C18 column was conditioned and activated with 10 mL of dichloromethane, followed by 10 mL of methanol and 10 mL of ultrapure water, without allowing the SPE cartridge to dry out. The entire 500 mL sample was passed through the column at the maximum allowable rate (approximately 5 mL/min). After each sample, 6 mL of water was used to elute polar impurities. Each water sample was percolated under a regulated vacuum so that the sample passed through the SPE cartridge under -20 bars until the cartridge was dried. The analytes were eluted from the SPE cartridge by 15 mL of dichloromethane at atmospheric pressure. The elution extract was concentrated to 1 mL under nitrogen at 30°C. Homogenization of the final extract was achieved with ultrasonic and vortex agitation [19].

2.3. GC/MS Analysis. The analysis of organics was conducted on gas chromatography (Agilent Technologies, 7890)

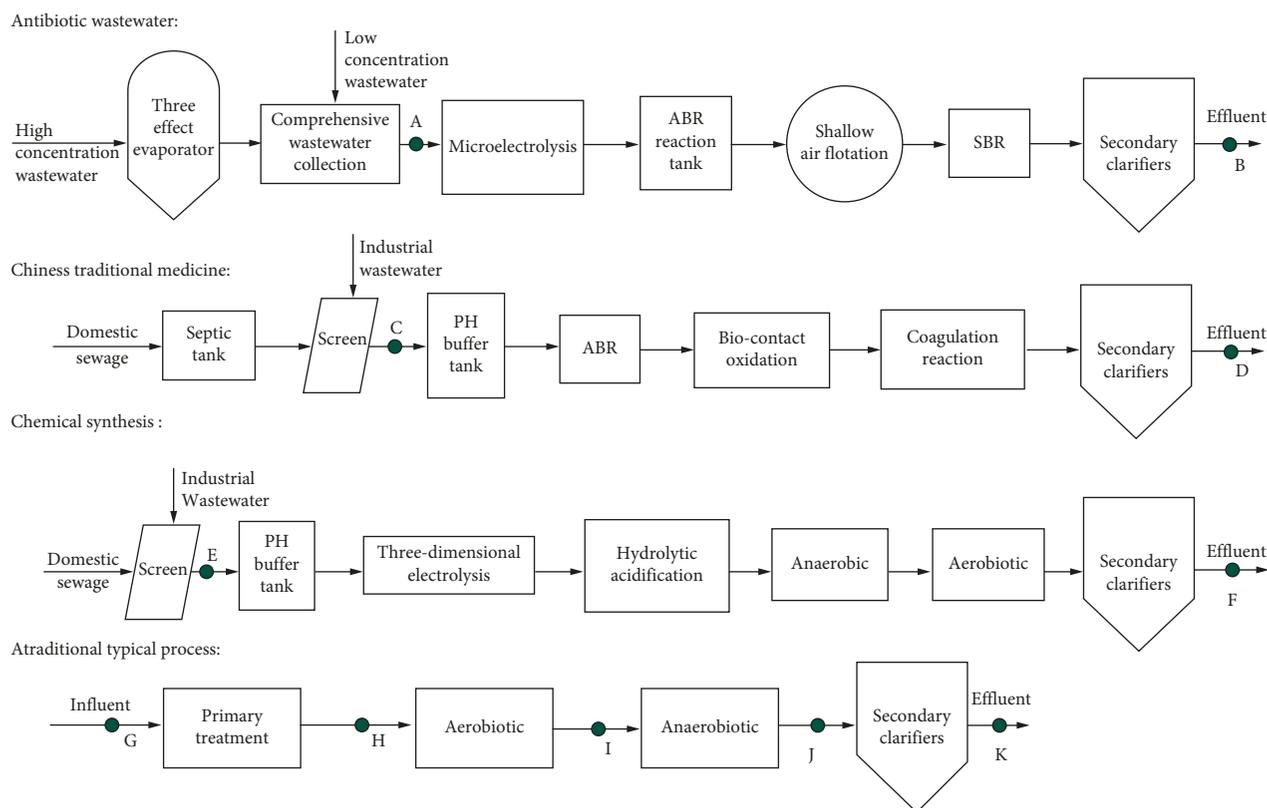


FIGURE 1: Schematic diagram of the treatment processes at three typical pharmaceutical wastewater treatment plants and the traditional typical process.

coupled with mass spectrometry under electron ionization (EI) mode (Agilent Technologies, 5977A) (GC-MS) in selective ion-monitoring mode. Splitless injection of a $1 \mu\text{L}$ sample was performed and followed with a 4 min solvent delay. The injector temperature was set at 250°C , and analytes were separated using a TR-5MS column ($30 \text{ m} \times 0.25 \text{ mm} \times 0.25 \mu\text{m}$ film thickness). Helium (99.999%) was used as carrier gas at a flow rate of $1 \text{ mL} \cdot \text{min}^{-1}$. The oven temperature was set to hold at 60°C for 4 min, ramped to 200°C at a rate of $5^\circ\text{C} \cdot \text{min}^{-1}$, and hold for 3 min, ramped to 300°C at a rate of $10^\circ\text{C} \cdot \text{min}^{-1}$ and hold for 2 min, and finally ramped to 325°C and hold for 3 min [20]. During analysis, quality assurance and quality control (QA/QC) were performed using procedural blanks, multilevel calibration curves ($R^2 = 0.999$), and calibration verification ($<5\%$). Each elution extract was analyzed in duplicate, and the average of three analyses was used.

The mass spectrometry system used here is equipped with a NIST11.L database. After the GC/MS measurement is completed, the system generates a list of possible organic compounds based on the mass spectral fragment peaks of each chromatographic peak. A substance is considered to have been identified when the ratio of peaks in its mass spectrum matches 90% or more of a standard mass spectrum. If the substance's mass spectrum matches less than 90% of all standard spectra after accounting for background values, the characteristic fragments and possible material structures corresponding to the peaks are identified and the organic compound is finally determined by examining the response signals of the fragment peaks in the actual

chromatogram. The classification of organic compounds separates compounds according to their functional groups: hydrocarbons, heterocycles, amines, acids, esters, ethers, alcohols, nitriles, aldehydes, phenols, organosilicon compounds, halohydrocarbons, and "other" compounds [21].

2.4. Relative Content Analysis. Although the number of organic compounds does not depend on the size of the molecules, it can still be a valuable part of quantitative analysis. In this study, the sum of the relative contents of the organic compounds is assumed to be 100% and the relative content of a substance is measured using the normalization method. Semiquantitative analysis and calculation of the relative content of each component were performed using peak areas and the following equation:

$$m_i = \frac{A_i}{\sum A_i} \times 100\%, \quad (1)$$

where m_i is the relative content (%) of component i and A_i is the peak area of component i . Through semiquantitative analysis of the peak areas, the relative contents of different organic compounds in the influent and effluent were determined.

2.5. Contribution to Pollution. The relative content of different organic compounds only indicates the proportion of total organic matter accounted for by each particular compound; thus, relative contents alone cannot determine

the degree to which a compound contributes to water pollution. The relative COD of an organic species was calculated by combining the relative content of the species with its theoretical oxygen demand (ThOD), which reflects the contribution of different organic pollutants to the total COD pollution load. According to the mathematical model of theoretical oxygen consumption of different organic compounds [22], the formula for calculating the oxygen demand per mole of organic compound is shown in the equation below, which assumes the molecular formula for organics is $C_aH_bO_cN_{(d_1+d_2)}S_eP_fCl_g$:

$$\text{ThOD} = \left(a + \frac{b}{4} - \frac{c}{2} + \frac{3}{4}d_2 + \frac{3}{2}d_1 + 2e + 2f \right) \times 32, \quad (2)$$

where $a, b, c, d_1, d_2, e, f, g$ represent the number of atoms of the corresponding element in the molecule; d_1 represents the number of nitrogen atoms from NO_3^- -N and NO_2^- -N; and d_2 represents other N atoms.

Zhao [23] proposed that the COD of a contaminant can be expressed as the product of its theoretical oxygen demand, ThOD, and its concentration:

$$\text{COD}_i = \text{ThOD}_i \times M \times K_i \times 1000, \quad (3)$$

where COD_i represents the theoretical COD value (mg/L) of organic compound i ; ThOD_i represents the theoretical oxygen demand (g/mol) of organic compound i ; M indicates the total concentration of organic matter in wastewater (mol/L); and K_i indicates the total proportion of organic compound i .

The contribution of different organic species to the COD can be represented by their proportion of the ThOD in the effluent. By combining GC/MS results with semiquantitative calculation theory, the concentration of an organic compound is proportional to its peak area. This means that the proportion of an organic compound in wastewater is the same as the ratio of its peak area relative to the total peak area. The COD of the different pollutants in the water samples were used to calculate the total COD with the following equation:

$$\text{COD}_g = \frac{\text{COD}_i}{\sum \text{COD}_i}. \quad (4)$$

3. Results and Discussion

3.1. Types of Refractory Organic Compounds in the Influent and Effluent of Typical Pharmaceutical Wastewater Treatment. The classes of refractory organic compounds found in the three types of typical pharmaceutical wastewater are shown in Figure 2. In the antibiotic pharmaceutical wastewater treatment plant, 53 organic compounds were detected in the influent while only 30 organic compounds were detected in effluent, which corresponds with a reduction of 43.40%. By contrast, in the pharmaceutical wastewater treatment plant used to treat traditional Chinese medicine, the effluent contained 25 more organic compounds than the influent; this indicated that, during the sewage treatment process, organic macromolecules are not

completely degraded into small organic molecules and thus a large number of refractory intermediates are present in the effluent. Small molecules produced during wastewater treatment can be bioutilized and form new metabolites that can be released into water [24]. The total number of organic compounds in the chemical synthesis pharmaceutical treatment plants exhibited little difference between influent and effluent.

In the influent and effluent of the antibiotic pharmaceutical wastewater treatment plant, hydrocarbons were the most frequently occurring class of organic compounds, with 20 compounds in the influent and 15 compounds in the effluent, accounting for 37.74% and 50.00% of the organic compounds, respectively. Acids, halogenated hydrocarbons, aldehydes, nitriles, and alcohols were detected in the influent while they were not detected in the effluent, and only one heterocyclic compound was found in the effluent while ten were present in the influent. This indicates that organic compounds containing halogenated hydrocarbons, aldehydes, nitriles, alcohols, and most heterocyclic compounds are easily degraded by microorganisms during wastewater treatment.

In the traditional Chinese medicine pharmaceutical wastewater treatment, organosilicon compounds were the most frequently detected class of organic compounds in the influent, comprising 36.67%, while 23 hydrocarbon compounds were identified in the effluent. Some refractory organics, including 4-hydroxypyridine-1-oxide, 4-nitrophthalhydrazide, diisobutyl phthalate, oleamide, stearylamide, etc., were still detected in the effluent after biological treatment, which indicates that these organics are not easily degraded. In the chemical synthesis, pharmaceutical wastewater, esters, and hydrocarbons were the most widely represented classes in the influent and effluent, respectively. Amines and heterocyclic organic compounds were detected in the influent but not the effluent, and alkanes were detected in the effluent but not the influent; this suggests that refractory amines and heterocyclic organic compounds may be degraded to form alkanes, which are relatively small compounds.

3.2. Relative Content of Refractory Organic Compounds in the Influent and Effluent of Typical Pharmaceutical Wastewater.

Figure 3 shows the relative content of different organic compound classes in the three types of typical pharmaceutical plants. Overall, the organic compound classes most frequently observed in the influent were heterocyclic compounds (30.24%), acids (63.65%), and esters (44.96%). In the effluent, the most frequently detected organic compound classes were organosilicon compounds (42.46%), esters (52.66%), and acids (62.54%).

In the antibiotic pharmaceutical wastewater influent, relatively high concentrations of 5-(phenylmethoxy)-1H-indole-3-carbaldehyde, amyl acetate, and *N,N*-dimethylformamide were observed: 15.86%, 22.28%, and 14.27%, respectively. However, these compounds were not detected in the effluent; rather, octamethylcyclotetrasiloxane, decamethylcyclopentasiloxane, and dodecyl mercaptan were

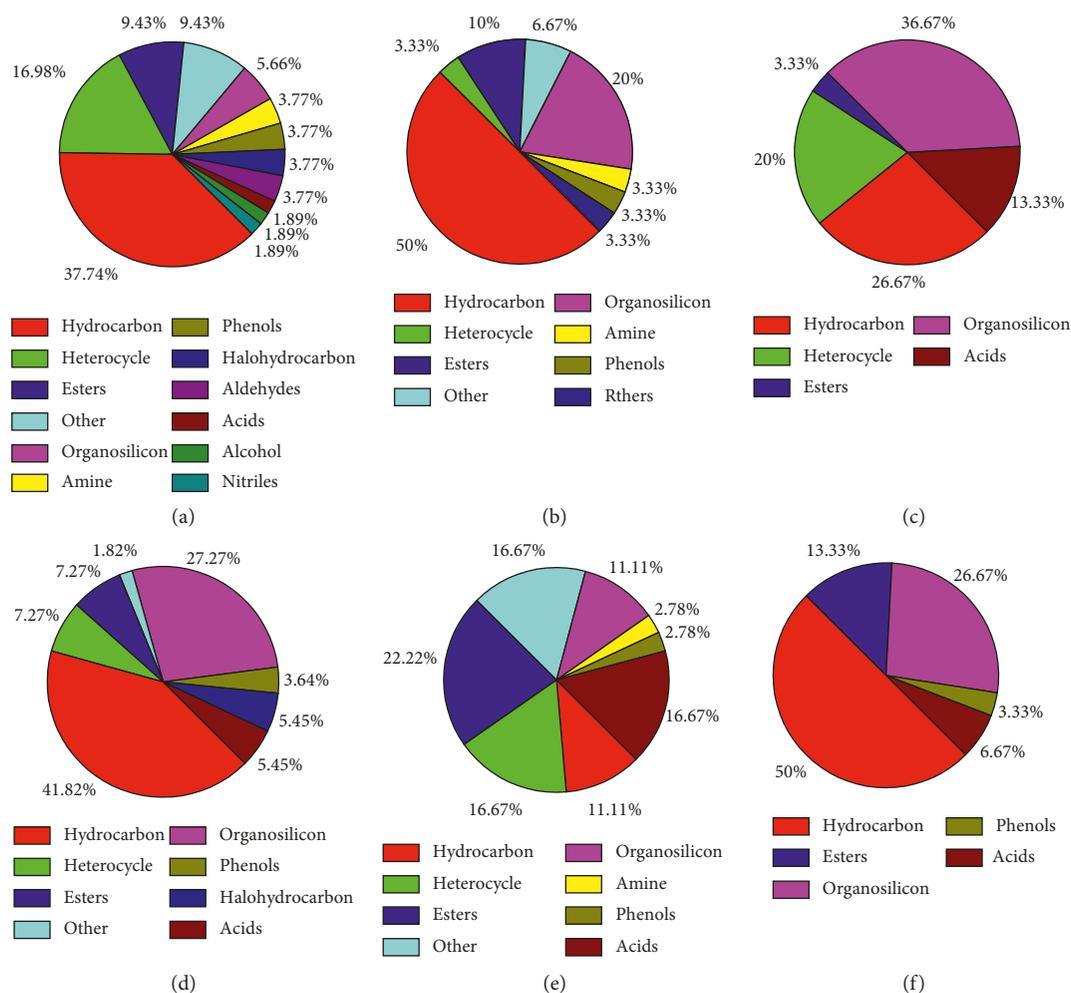


FIGURE 2: Distributions of the classes of refractory organic compounds in the influent and effluent from three types of typical pharmaceutical wastewater treatment plants: (a), (c), and (e) represent the influent of antibiotic wastewater, Chinese traditional medicine wastewater, and chemical synthesis wastewater, respectively; (b), (d), and (f) represent the corresponding effluent.

found at high relative concentrations in the effluent. These three compounds comprised 46.97% of the organics present in the effluent, but only accounted for 7.62% of the organics in the influent. This can be explained by taking into account the fact that the relative content of organics depended on the efficiency of the removal and treatment processes.

In the traditional Chinese medicine pharmaceutical wastewater, the relative contents of acids and esters were significantly different in the influent and effluent. Acids accounted for 63.65% of the organics present in the influent, whereas they only accounted for 25.73% of the organics in the effluent. Conversely, esters comprised 2.31% of the organics in the influent and 52.66% of organics in the effluent. Oleamide had the highest relative content of organics in the influent, 47.20%, and was still present at a high relative content in the effluent, 24.38%. Therefore, characterizing the occurrence and fate of oleamide in wastewater is crucial in order to determine how to decrease its discharge into water bodies in the environment. In addition to oleamide, the relative contents of di-*n*-octyl phthalate and di(2-ethylhexyl) adipate in the effluent were also high, together accounting for 76.43% of the organics.

The four compounds comprising the highest percentage of organics in chemical synthesis wastewater influent were butyl butyrate (24.48%), 4,7-dichloroquinoline (17.15%), ethyl *p*-nitrobenzoate (17.11%), and 1-(3-nitrophenyl)acetone (11.99%). Oleamide had the highest relative content in the effluent at 60.14%, while it only accounted for 2.54% in the influent.

The relative content is not related to the number of organic compounds in a particular class. For example, in antibiotics pharmaceutical wastewater, the class with the largest number of organic compounds in the influent and effluent was the hydrocarbon class, yet heterocyclic rings and organosilicon compounds were the classes with the highest relative content in the influent and effluent, respectively.

3.3. Contribution of Refractory Organic Compound Classes to Pollution in Typical Pharmaceutical Wastewater. The relative content of an organic compound only indicates the content of that compound relative to all of the organic compounds that are present; relative content does not indicate the degree to which a compound contributes to water pollution.

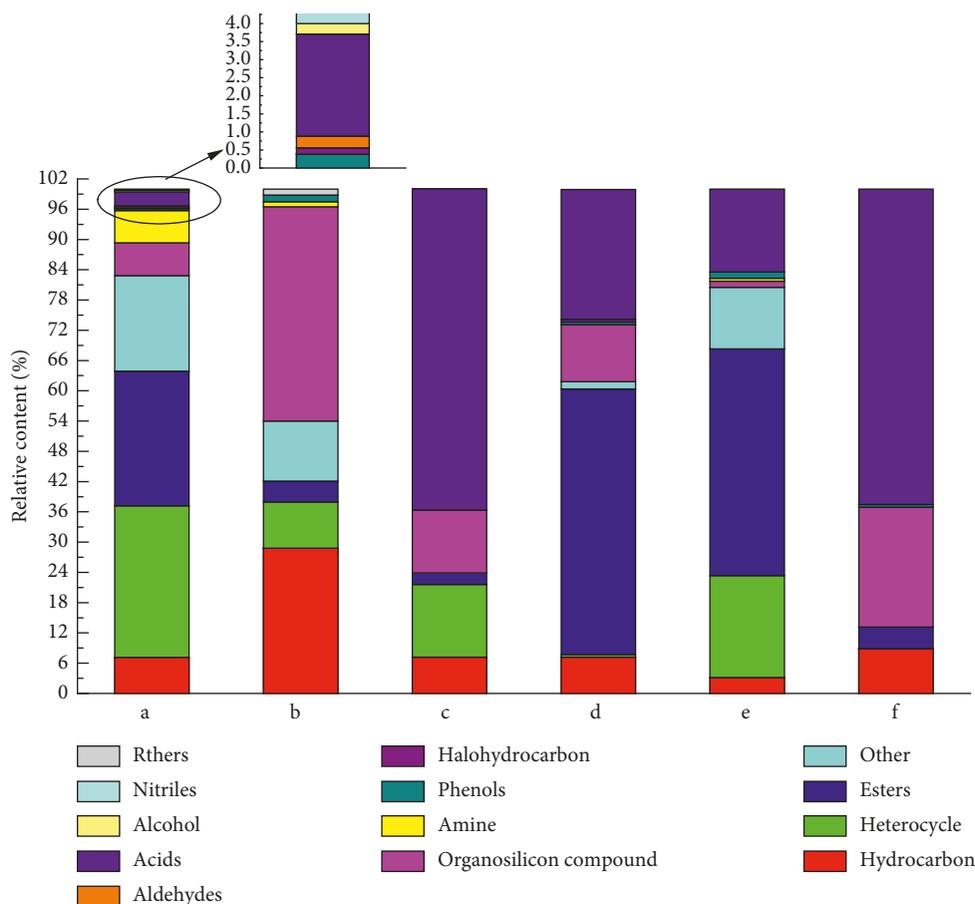


FIGURE 3: Relative contents of the classes refractory organic compounds in three types of typical pharmaceutical wastewater: (a), (c), and (e) represent the influent of antibiotic wastewater, Chinese traditional medicine wastewater, and chemical synthesis wastewater, respectively; (b), (d), and (f) represent the corresponding effluent.

Evaluating a compound's contribution to pollution is one of the key steps towards understanding the relative occurrence and fate of organic compounds in wastewater. Figure 4 depicts the contribution of different organic compound classes to pollution in three types of typical pharmaceutical wastewater. In the influent, the organic compound classes contributing the most to pollution were acids (35.23%), esters (67.22%), and heterocyclic compounds (41.24%). In the effluent, the organic compound classes with the largest contribution to the COD were acids (37.45%), esters (59.02%), and organosilicon compounds (65.13%). These results are consistent with those obtained from the relative content experiment. For instance, in the influent of antibiotic pharmaceutical wastewater, the organic compounds with relative contents greater than 10% were 5-(phenylmethoxy)-1*H*-indole-3-carbaldehyde, amyl acetate, and *N,N*-dibenzylethylenediamine, and these compounds also contributed to greater than 10% of the pollution. In the effluent of chemical synthesis wastewater, oleamide not only had the highest relative content (60.14%), but it also had the highest pollution contribution (62.87%). Overall, it was observed that the pollution contribution of an organic compound was directly proportional to its relative content; the organic compounds with high relative contents also exhibited high pollution contribution.

3.4. Case Analysis of a Typical Wastewater Treatment Process. Analyzing the organic matter in the influent and effluent of pharmaceutical wastewater is not sufficient to understand the efficiency of refractory organic matter removal at each treatment stage in a wastewater treatment system. Therefore, the classes and distribution of PhACs and the occurrence and fate of these organic compounds were investigated in a representative pharmaceutical factory with the typical traditional treatment process of "primary treatment + anaerobic + aerobic + sedimentation" during the various stages in the treatment system. Prior to analysis, the relative molecular weights of organic compounds were used to predict structural changes and qualitatively determine changes in degradability.

3.5. Distribution of Organic Compound Classes at Each Stage of a Typical Traditional Treatment Process. Figure 5 displays the distribution of the classes of organic compounds detected during the different stages of wastewater treatment. As the wastewater passed through the stages of treatment, the amount of hydrocarbons increased while the amount of heterocycles, esters, acids, and class categorized as "other" decreased. The pharmaceutical compounds observed during the primary treatment were different from those observed in the secondary settling tank.

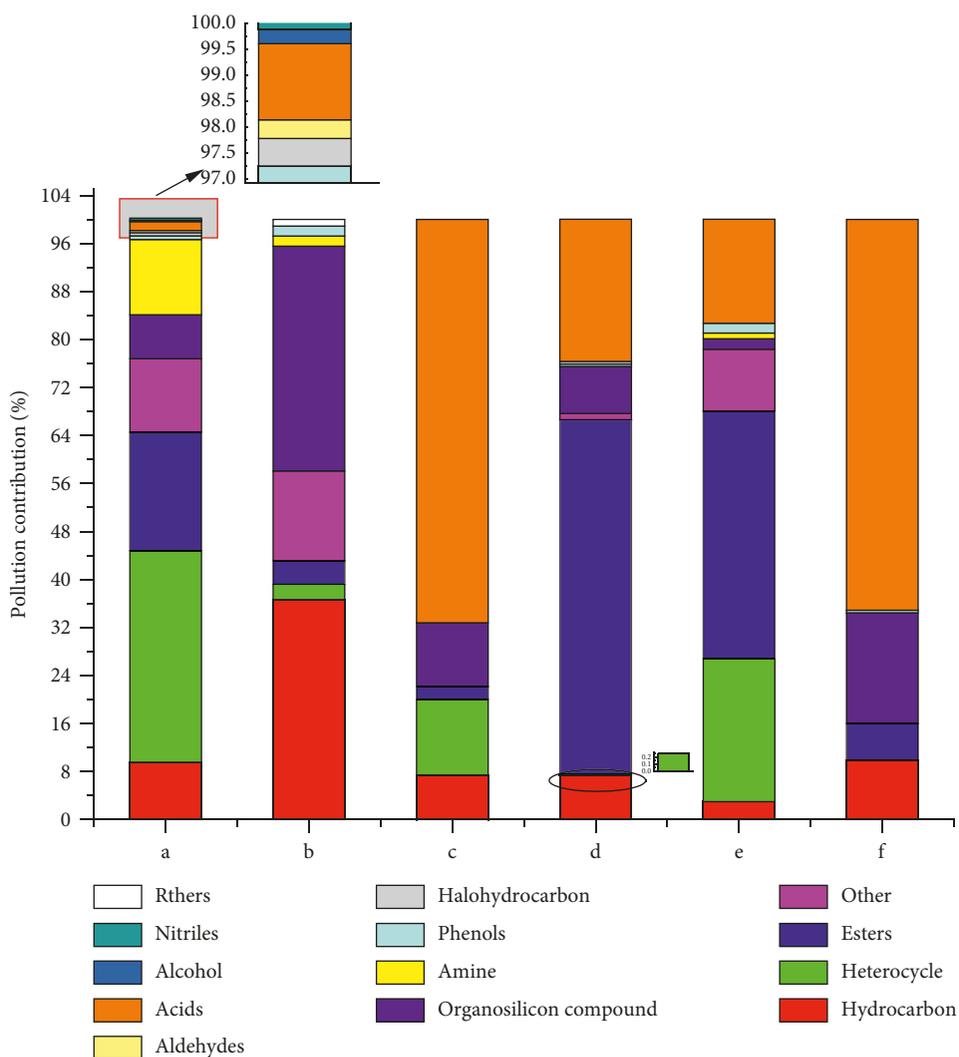


FIGURE 4: Distributions of the pollution contribution of the classes of refractory organic compounds in three types of typical pharmaceutical wastewater: (a), (c), and (e) represent the influent of antibiotic wastewater, Chinese traditional medicine wastewater, and chemical synthesis wastewater, respectively; (b), (d), and (f) represent the corresponding effluent.

For example, there were only four hydrocarbon compounds after the primary treatment while there were 21 in the second settling tank, and 11 heterocyclic compounds were observed after the primary treatment while none were detected in the second settling tank. This could be due to the different physicochemical characteristics of these compounds and the different composition of the primary and secondary sedimentation wastewater, both of which could result in different removal efficiencies. There were four kinds of organic compounds present in the wastewater treatment process, namely, *N,N*-dimethylformamide, 4-methyloctane, *N*-ethylmorpholine, and 4-amino-*N,N*-diethylbenzamide. The presence of these compounds indicates that they are refractory and are not degraded by microorganisms; thus, they may be discharged into the aquatic environment.

3.6. Relative Content of Organic Compound Classes during Each Stage of a Typical Traditional Treatment Process. The relative contents of the classes of organic compounds

detected during the treatment stages are shown in Figure 6. These results demonstrate that the relative content of amines increased by 16.32% during the primary treatment step, whereas the other organic compound classes showed either little to no increase or a slight reduction. After anaerobic treatment, the relative contents of heterocycles and “other” compounds reduced by 8.93% and 15.72%, respectively, and during sedimentation, a large increase in hydrocarbons was observed (68.97%) while no reduction observed for esters and acids. Overall, many of the classes of organic compounds, including organosilicon compounds, acids, esters, heterocycles, alcohols, and “other” compounds, were effectively biodegraded and the concentrations of their transformation products (hydrocarbons) were relatively high in the effluent.

3.7. Relative Molecular Weight Classes during Each Stage of a Typical Traditional Treatment Process. The relative distributions of molecular weight classes during each stage of

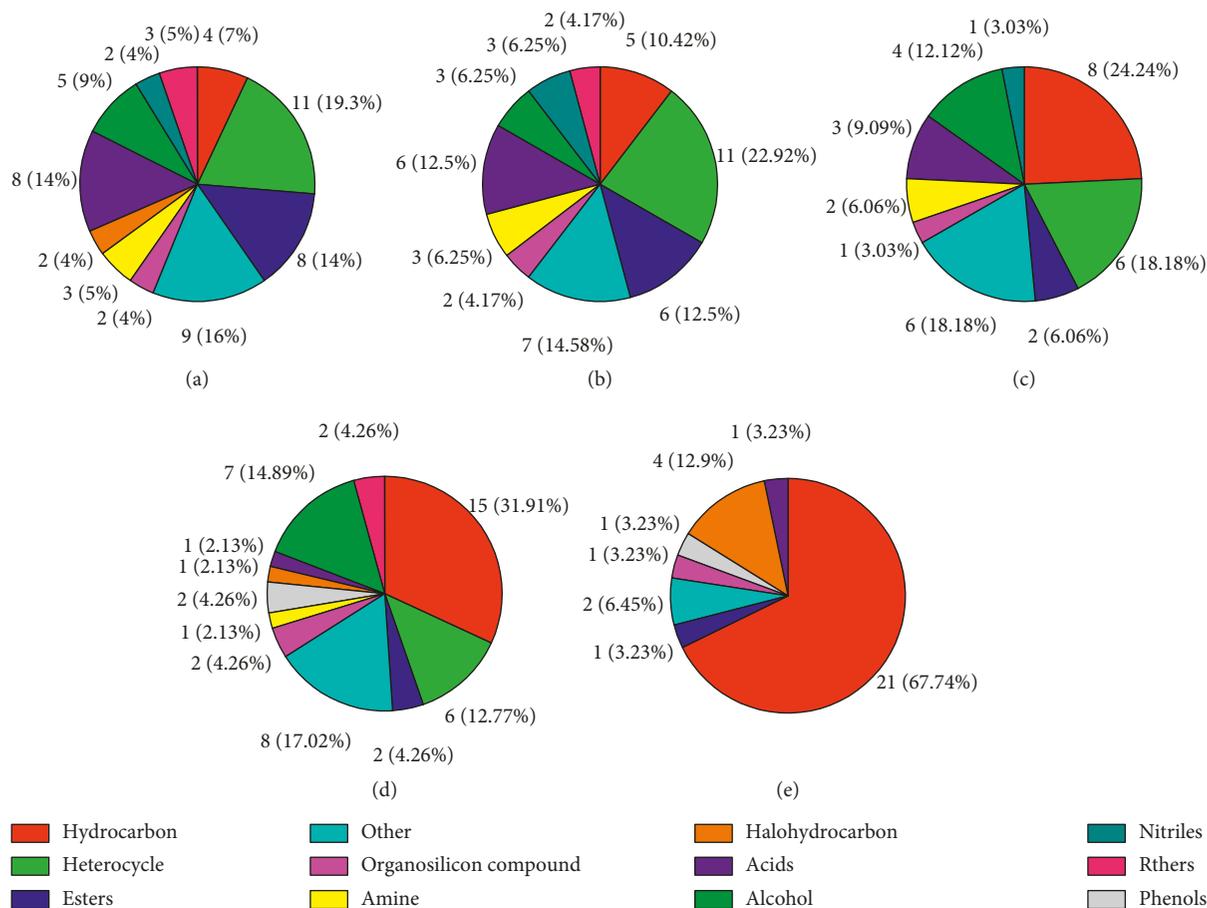


FIGURE 5: Distributions of organic compound classes during each stage of a typical traditional treatment process. (a) Raw water, (b) primary treatment, (c) anaerobic, (d) aerobic, (e) sediment.

a typical traditional treatment process are shown in Figure 7. The molecular weights of the organic compounds in wastewater are not uniformly distributed across the stages of the treatment process. Overall, organic compounds with molecular weights between 100 and 150 Da had the largest relative content during each treatment stage; this molecular weight classes accounted for 45.61% of the raw water stage, 37.5% of the primary treatment stage, 45.45% of the anaerobic stage, and 41.3% of the aerobic stage. The results show that the relative content of organic compounds with a molecular weight less than 150 Da decreased during the primary treatment step, whereas organic compounds with a molecular weight greater than 150 Da increased. This may be the result of macromolecules degrading into small molecules during the treatment process.

3.8. Process Improvement. The class, relative content, and contribution to pollution of organic compounds were studied in the influent and effluent of three types of typical pharmaceutical wastewater. Process improvements that were added to the sewage treatment process are shown as red shapes in Figure 8. The antibiotic pharmaceutical wastewater treatment had three main problems in the process: (1) High-concentration wastewater completely evaporates and the

operational costs are very high. Thus, the improved process can divert high-concentration wastewater so that part of it is mixed with low-concentration wastewater in the treatment system and part of it evaporates. (2) In the effluent, refractory organics with a benzene ring and a heterocyclic functional group account for 17.32% of the organics. These refractory organics are also detected in the influent; this indicates that the main microelectrolysis process, which generates hydroxyl radicals, cannot effectively treat these compounds. Therefore, the improved process has replaced the microelectrolysis stage with a strong electrocatalytic device that uses an external power source to generate an electric field while the strong oxidizing particles ($\cdot\text{OH}$, O_2 , H_2O_2 , etc.) generated by the electrocatalytic reaction are rapidly and indiscriminately chain-reacted with organic pollutants in the wastewater. The refractory organic compounds that contain a benzene ring and a heterocyclic ring structure were oxidatively degraded by the electrocatalytic treatment [25]. (3) An acidizing cell was added to the treatment process in order to adjust the pH during the microelectrolysis stage and a UASB anaerobic reactor was added to simultaneously increase the COD and salinity removal rate of wastewater [26].

The wastewater in traditional Chinese medicine pharmaceutical wastewater treatment is less biodegradable; thus,

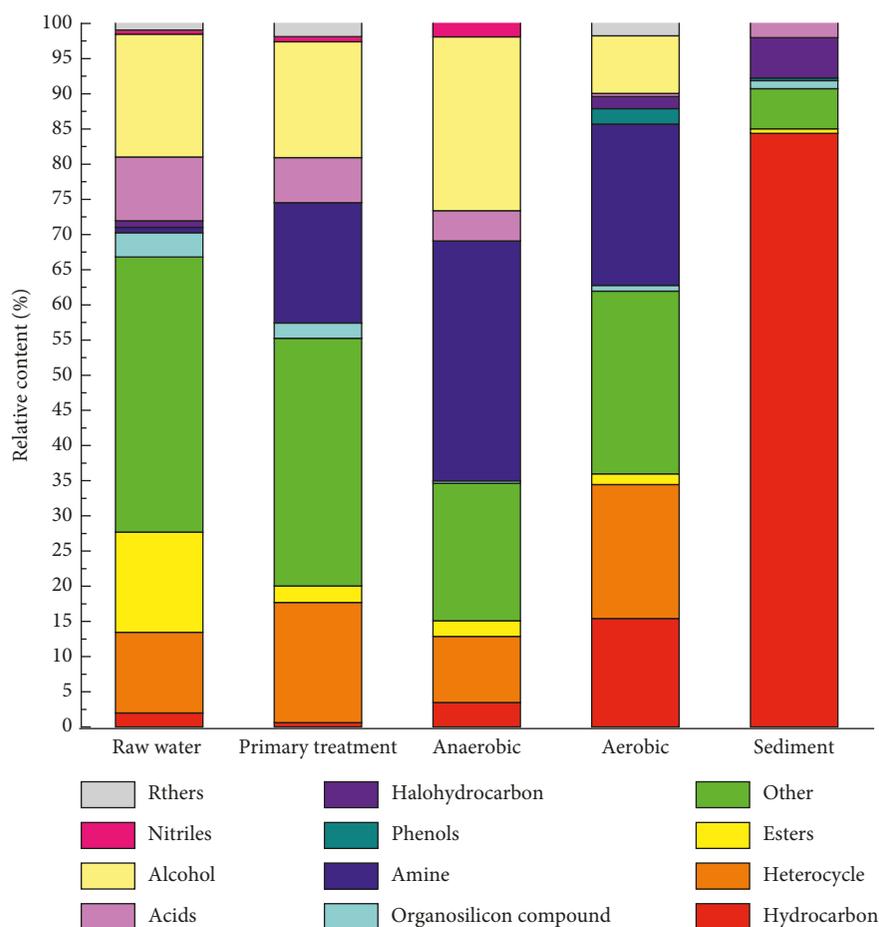


FIGURE 6: Relative contents of organic compound classes during each stage of typical traditional treatment process.

it is conceivable to add a hydrolysis acidification tank, which can convert refractory organic matter in the raw wastewater into biodegradable organic matter. This improvement to the biodegradability of the wastewater improves the efficiency of wastewater treatment in the subsequent biochemical treatment and ultimately reduces the concentration of pollutants in the wastewater. Furthermore, the ABR reactor used in the original process is not deep enough and the influent water is not well-mixed; therefore, the first grid of the ABR reactor is subjected to a local load greater than the average load, which decreases the treatment efficiency. When Zhao [19] used an “ABR-UASB-biological contact oxidation” process to treat wastewater, the results demonstrated that the removal rates of COD, suspended solid (SS), and $\text{NH}_3\text{-N}$ could reach 95.2%, 90.0%, and 71.4%, respectively.

In the chemical synthesis pharmaceutical wastewater treatment process, the removal of organic pollutants is generally good, although the concentrations of COD and total nitrogen (TN) in effluent do not reach the standard. Hence, compound microorganisms were added to the process to improve the purification of wastewater because they exhibit strong functionality and high economic efficiency. Yang Guifang demonstrated that treating pharmaceutical wastewater with composite microorganisms (photosynthetic bacteria, *Bacillus subtilis*, and denitrifying bacteria) decreased the

TN in the wastewater by 92.5%, the COD by 79.5%, and the chroma by 74.5% [27].

4. Conclusions

The class, relative content, and contribution to pollution of refractory organic compounds were studied in the influent and effluent of three types of typical pharmaceutical wastewater and a representative pharmaceutical factory with the typical traditional treatment process of “primary treatment + anaerobic + aerobic + sedimentation”. The results revealed that the relative contents of organic compound classes in wastewater are not related to the number of organic compounds, but are related to the overall pollution contribution. Generally, the predominant fate of organics was biodegradation; most organics were effectively degraded after biological treatment, which was reflected in the increase of the number of alkanes in effluent. However, some organic compounds were present in both the influent and effluent, and thus analysis of their transformation products is recommended. In the typical traditional treatment process, four organic compounds *N,N*-dimethylformamide, 4-methyloctane, *N*-ethylmorpholine, and 4-amino-*N,N*-diethylbenzamide were present throughout the wastewater treatment process and were consequently released to the environment.

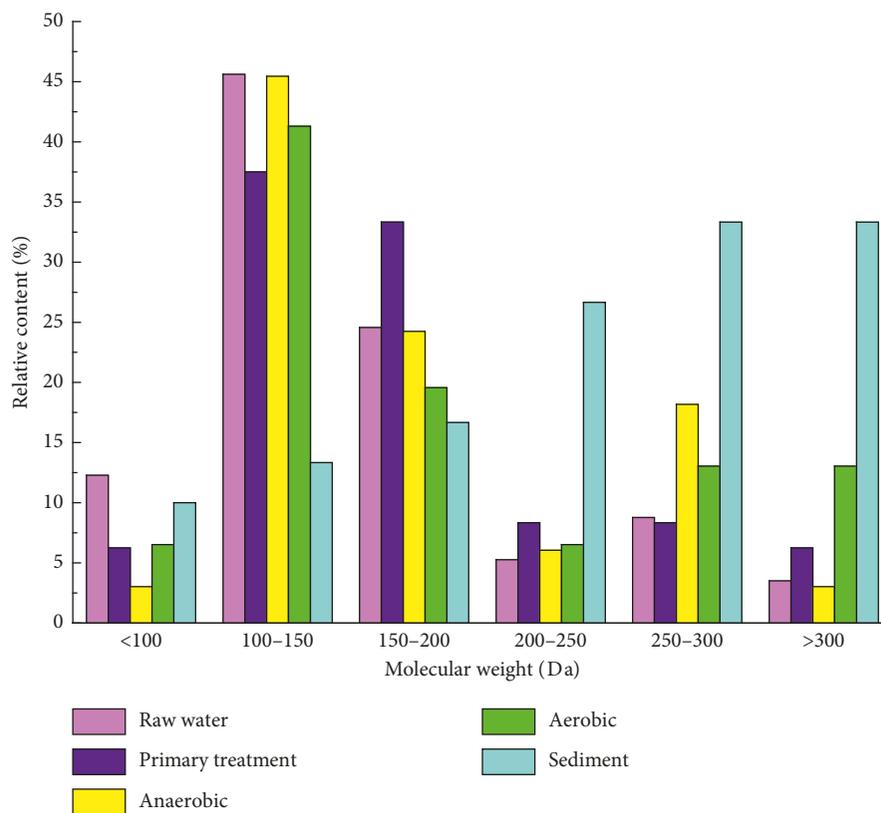


FIGURE 7: Relative distributions of molecular weight classes during each stage of a typical traditional treatment process.

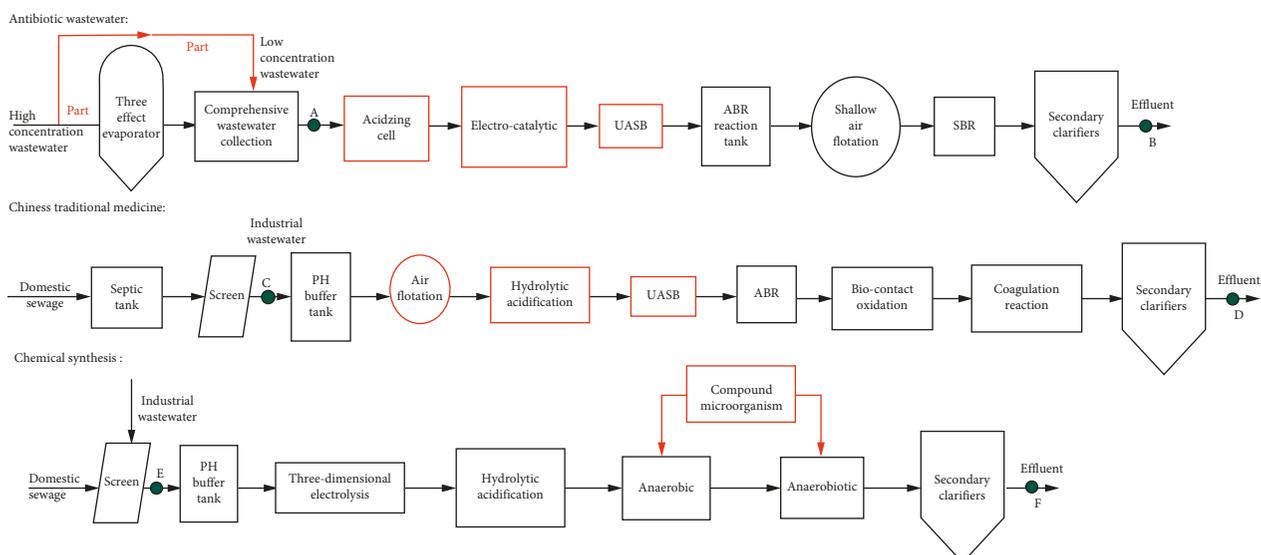


FIGURE 8: Schematic diagram of the improved processes developed for the three typical pharmaceutical wastewater treatment plants. Improvements to the process are indicated by the color red.

A specific, goal-oriented, and class-specific treatment strategy to optimize the treatment process and minimize resource and energy consumption was developed based on the composition, distribution, and fate of PhACs during wastewater treatment. However, some organic compounds persisted throughout the chemically assisted primary treatment and biological treatment processes and were

found in effluents. Additionally, since PhACs have different chemical properties, the suspended solids in the influent and effluent should be analyzed along with the aqueous phase in order to gain a better understanding of fate and behaviour of PhACs.

In this study, qualitative and semiquantitative measurements of organic compounds were conducted on

pharmaceutical wastewater. However, the degradation mechanisms of refractory organics in different types of wastewater have not been thoroughly studied. Considering the toxicity of some organic compounds, future studies should pursue quantitative measurements in order to determine how to prevent harmful organic compounds from reaching toxic concentrations in the environment. In order to achieve a better understanding of the fate of PhACs and their release to the environment, further investigation of the transformation products from wastewater treatment is needed.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this article.

Authors' Contributions

Qiao Luo and Jing Wang contributed equally to this work. Qiao Luo did the experiment and wrote the paper. Yu Shen and Peng Yan designed the experiment scheme. YouPeng Chen modified the paper. Jing Wang and JianHui Wang performed the data analysis and Jing Wang wrote the revised part of the paper. ChengCheng Zhang did some experiment.

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References

- [1] IMS Health Canada, "Unlocking the value of health information," 2012, <http://www.imshealthcanada.com>.
- [2] Q. Yan, X. Gao, Y.-P. Chen et al., "Occurrence, fate and ecotoxicological assessment of pharmaceutically active compounds in wastewater and sludge from wastewater treatment plants in Chongqing, the Three Gorges Reservoir Area," *Science of The Total Environment*, vol. 470-471, pp. 618-630, 2014.
- [3] S. Karthikeyan, M. Anil Kumar, P. Maharaja, T. Partheeban, J. Sridevi, and G. Sekaran, "Process optimization for the treatment of pharmaceutical wastewater catalyzed by poly sulphate sponge," *Journal of the Taiwan Institute of Chemical Engineers*, vol. 45, no. 4, pp. 1739-1747, 2014.
- [4] Q. Yan, X. Gao, L. Huang et al., "Occurrence and fate of pharmaceutically active compounds in the largest municipal wastewater treatment plant in Southwest China: mass balance analysis and consumption back-calculated model," *Chemosphere*, vol. 99, pp. 160-170, 2014.
- [5] L. Gao, Y. Shi, W. Li, H. Niu, J. Liu, and Y. Cai, "Occurrence of antibiotics in eight sewage treatment plants in Beijing, China," *Chemosphere*, vol. 86, no. 6, pp. 665-671, 2012.
- [6] A. Jelic, M. Gros, A. Ginebreda et al., "Occurrence, partition and removal of pharmaceuticals in sewage water and sludge during wastewater treatment," *Water Research*, vol. 45, no. 3, pp. 1165-1176, 2011.
- [7] A. Dirany, S. Efreanova Aaron, N. Oturan, I. Sirés, M. A. Oturan, and J. J. Aaron, "Study of the toxicity of sulfamethoxazole and its degradation products in water by a bioluminescence method during application of the electro-Fenton treatment," *Analytical and Bioanalytical Chemistry*, vol. 400, no. 2, pp. 353-360, 2011.
- [8] J. L. Martinez, "Antibiotics and antibiotic resistance genes in natural environments," *Science*, vol. 321, no. 5887, pp. 365-367, 2008.
- [9] F. Pomati, C. J. Cotsapas, S. Castiglioni, E. Zuccato, and D. Calamari, "Gene expression profiles in zebrafish (*Danio rerio*) liver cells exposed to a mixture of pharmaceuticals at environmentally relevant concentrations," *Chemosphere*, vol. 70, no. 1, pp. 65-73, 2007.
- [10] Y. L. Zhou, W. U. Qing, and M. U. Yi-Zhou, "Analysis of the toxic organic matters in the yellow river basin and the concerned countermeasures," *Hydrology*, vol. 24, no. 6, 2004.
- [11] E. R. Cooper, T. C. Siewicki, and K. Phillips, "Preliminary risk assessment database and risk ranking of pharmaceuticals in the environment," *Science of The Total Environment*, vol. 398, no. 1-3, pp. 26-33, 2008.
- [12] A. Jelic, F. Fatone, S. Di Fabio, M. Petrovic, F. Cecchi, and D. Barcelo, "Tracing pharmaceuticals in a municipal plant for integrated wastewater and organic solid waste treatment," *Science of The Total Environment*, vol. 433, pp. 352-361, 2012.
- [13] H. Olvera-Vargas, N. Oturan, M. A. Oturan, and E. Brillas, "Electro-Fenton and solar photoelectro-Fenton treatments of the pharmaceutical ranitidine in pre-pilot flow plant scale," *Separation and Purification Technology*, vol. 146, pp. 127-135, 2015.
- [14] F. J. Beltrán, A. Aguinaco, J. F. García-Araya, and A. Oropesa, "Ozone and photocatalytic processes to remove the antibiotic sulfamethoxazole from water," *Water Research*, vol. 42, no. 14, pp. 3799-3808, 2008.
- [15] S. Chelliapan and P. J. Sallis, "Removal of organic compound from pharmaceutical wastewater using advanced oxidation processes," *Journal of Scientific and Industrial Research*, vol. 72, pp. 248-254, 2011.
- [16] R. Uchida, M. Kubota, H. Matsuda, and N. Uemura, "Oxidative decomposition and mineralization of refractory pharmaceutical products using persulfate," *Journal of the Japan Society of Material Cycles and Waste Management*, vol. 24, no. 6, pp. 125-132, 2013.
- [17] A. Liu, S. Zhang, L. Huang et al., "Electrochemical oxidation of luteolin at a glassy carbon electrode and its application in pharmaceutical analysis," *Chemical and Pharmaceutical Bulletin*, vol. 56, no. 6, pp. 745-748, 2008.
- [18] B. Wang, X. Chang, and H. Ma, "Electrochemical oxidation of refractory organics in the coking wastewater and chemical oxygen demand (COD) removal under extremely mild conditions," *Industrial & Engineering Chemistry Research*, vol. 47, no. 21, pp. 8478-8483, 2008.
- [19] Y. Zhang, Z. Xiao, S. Lv, Z. Du, and X. Liu, "Simultaneous determination of 16 polycyclic aromatic hydrocarbons in reclaimed water using solid-phase extraction followed by ultra-performance convergence chromatography with photodiode array detection," *Journal of Separation Science*, vol. 39, no. 5, pp. 993-999, 2016.
- [20] R. He, Y. Li, P. Xiang et al., "Organophosphorus flame retardants and phthalate esters in indoor dust from different

- microenvironments: bioaccessibility and risk assessment," *Chemosphere*, vol. 150, pp. 528–535, 2016.
- [21] J. F. M. McOmie, "Protective Groups in Organic Chemistry," Plenum Press, New York, NY, USA, 1973.
- [22] C. Huang, "Mathematical calculation models of the theoretical chemical oxygen demand for different types of organic compounds," *China Environmentalence*, vol. 17, no. 2, 1997.
- [23] J. Zhao, *Degradation Performance and Mechanism Study of DBP Advanced Treated by Compositied Process of O3/GAC/H2O2*, Harbin University of Industry, Harbin, China, 2013.
- [24] P. Jin, Y. Shi, and W. Ren, "Transformation characteristics of dissolved organic matter in process of wastewater treatment," *Chinese Journal of Environmental Engineering*, vol. 9, no. 1, pp. 1–6, 2015.
- [25] X. Mf, *Electrocatalytic Oxidation Mechanism and Application of Refractory Organic Pollutants*, Nanjing University, Nanjing, China, 2013.
- [26] Y. Li, J. Ma, B. Feng, J. Yu, and W. Yang, "Experimental study on pharmaceutical wastewater treated by UASB anaerobic reactor," *Environmental Science and Management*, vol. 36, no. 9, 2011.
- [27] G. Yang, R. Wang, J. Lu et al., "The purification effect of compound micoorganisms on pharmaceutical wastewater," *Journal of Xinyang Normal University*, vol. 27, no. 4, 2014.



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