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Ultraviolet-coupled advanced oxidation processes for anti-COVID-19 drugs treatment: Degradation mechanisms, transformation products and toxicity evolution

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HIGHLIGHTS

- Decomposition kinetics and optimal reaction conditions during UV/AOPs for anti-COVID-19 drugs.
- 24 TPs and degradation pathways were proposed by DFT and QTOF.
- Toxicity data of RDV in QSAR was supplemented by luminescent bacterial test.
- Combined QSAR prediction, luminescent bacterial tests and TPs peak area evolution to analyze TPs' toxicity.
- Halogen groups contributed to the TPs' toxicity of HCQ.

ABSTRACT

Remdesivir (RDV), dexamethasone (DEX) and hydroxychloroquine (HCQ) were widely used in the treatment of COVID-19 pneumonia, possibly causing environmental risks and drug-resistance viruses. This study elucidated the degradation mechanisms and potential toxicity risks of the three anti-COVID-19 drugs by UV and ultraviolet-coupled advanced oxidation processes (UV/AOPs). All the drugs could be degraded by more than 98% within 3 min under the following optimal conditions: pH of 5.0 and drug-to-oxidant (H₂O₂) molar ratio of 1:200. Combined with density functional theory (DFT) analysis and high-performance liquid chromatography quadrupole time-of-flight mass spectrometry (HPLC-QTOF-MS), twenty-four transformation products (TPs) were detected and the main degradation pathways were investigated. Based on bacterial luminescence inhibition test and the peak-area evolution of TPs, RDV and HCQ showed an obvious toxicity-increase region when TPs were generated in large quantities, while the toxicity of DEX continued to decline during degradation processes. By QSAR predictions, the main contributors to the toxicity evolution during the UV/AOPs were predicted. Halogen-containing TPs showed significantly higher toxicity than other TPs, and thus the chlorine-containing structure in HCQ presented the potential toxicity. Appropriate reaction parameters and adequate reaction time for the UV/AOPs could eliminate the toxicity of TPs and ensure environmental safety. This study could play a positive role in the treatment of anti-COVID-19 drugs and their environmental hazard assessment.

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https://doi.org/10.1016/j.chemosphere.2022.134968
Received 10 March 2022; Received in revised form 6 May 2022; Accepted 11 May 2022
Available online 14 May 2022
0045-6535/© 2022 Published by Elsevier Ltd.
1. Introduction

According to statistics released by Johns Hopkins University in the US, there were about 514,505,453 confirmed cases of COVID-19 with a total of 6,256,082 deaths worldwide as of May 5, 2022, as a result of the outbreak of COVID-19 around the world (Yang et al.; Dong et al., 2020). Remdesivir (RDV), dexamethasone (DEX) and hydroxychloroquine (HCQ) were included in COVID-19 disease therapeutic guidelines in many countries (Dehelean et al., 2020; Galani et al., 2021). Therefore, they entered natural water from medical use, drug disposal and incomplete metabolism and they were frequently detected in the aquatic environment (Ncube et al., 2018; Sugihara, 2018; Huang et al., 2020; Namou et al., 2020). However, they were difficult to be removed by traditional wastewater treatment plant processes (Kuroda et al., 2021). The long-term existence of these drugs in the environment would not only pose a serious threat to biological health but also enhance the drug resistance of the COVID-19 virus, resulting in a reduction in the performance of anti-COVID-19 drugs (Dong et al., 2020b; Kumar et al., 2020; Kuroda et al., 2021). What’s worse, few studies were found on the degradation and fate of anti-COVID-19 drugs, so a technique to remove anti-COVID-19 drugs and limit environmental exposure was of great importance.

RDV, DEX and HCQ were recommended by the FDA, WHO and other organisations as effective anti-COVID-19 drugs (Ahmed and Hassan, 2020; Rubin et al., 2020; Wise, 2020), which resulted in their more widespread use in the treatment of COVID-19 patients (The RECOVERY Collaborative Group, 2021; Huang et al., 2020; Sterne et al., 2020; Wang et al., 2020; Yao et al., 2020; Skipper and Boulware, 2021). However, the high stability, bioaccumulation and toxicity of transformation products (TPs) caused the accumulation of these drugs in the environment, posing an environmental risk (Dabic et al., 2019; Bensalah et al., 2020). From the latest studies, RDV generated new TPs during degradation and metabolism, and all of them could not be eliminated completely and discharged into the water (Hu et al., 2021; Dadinaboyna et al., 2021). Meanwhile, DEX was frequently detected in medical wastewater as a commonly used glucocorticoid. Moreover, the toxicity of HCQ to aquatic animals had also been reported (Guo et al., 2017; Li et al., 2022).

Ultraviolet-coupled advanced oxidation processes (UV/AOPs) were the superior technology for the degradation of pharmaceuticals (Chu et al., 2016; Liu et al., 2020; She et al., 2021; Guo et al., 2022). As newly developed antiviral drugs, the studies on RDV were paid more attention to the toxicity of the metabolites, and less to the TPs produced by AOPs (Zhao et al., 2020). Kargar et al. found HCQ could be effectively degraded with a combination of titanium oxide (Kargar et al., 2019b). Kargar et al. found HCQ could be efficiently photodegraded with a combination of titanium oxide (Kargar et al., 2021). Bensalah found electrochemical advanced oxidation technology could efficiently degrade HCQ (Bensalah et al., 2020). As one of UV/AOPs technology, the UV/H₂O₂ process could effectively degrade PPCPs, because the rate constants (k) reacting with HO• were as high as 10⁻²⁻⁻¹ M⁻¹ s⁻¹ (Guo et al., 2018b). It had mature industrial application capabilities because of the characteristics of high-efficiency and low-consumption (Anjali and Shanthakumar, 2019; Sanganyado and Gwenz, 2019). During UV/H₂O₂ process, UV light could excite H₂O₂ to generate hydroxyl radicals (HO•), which reacted non-selectively with organics and reduced drugs concentration (Somathilake et al., 2019). Therefore, UV/H₂O₂ is an efficient technology in minimizing anti-COVID-19 drug micro-pollution (Zhang et al., 2015).

However, the degradation of pharmaceuticals did not exactly equal toxicity reduction (Ebele et al., 2017). In most cases, TPs could not be completely degraded and flow into the aquatic environment, becoming the major contributors of biotoxicity (Hong et al., 2020). Therefore, the toxicity of TPs generated during the UV/AOPs should be evaluated to ensure applicability and safety. Most drugs have undergone rigorous human toxicity assessments but their potential toxicity to the environment is insufficient. Due to the high sensitivity of luminescent bacterial test, it is suitable for determining environmental toxicity evolution during the advanced oxidation processes (Gmurek et al., 2015; Westphal et al., 2020).

In this study, the degradation kinetics of three anti-COVID-19 drugs, namely, RDV, DEX and HCQ were evaluated under different conditions to confirm the optimal reaction parameters. High-performance liquid chromatography coupled with quadrupole time-of-flight mass spectrometry (HPLC-QTOF-MS) detection and density functional theory (DFT) calculation were used to determine their degradation pathways and TPs. Finally, the evolution of toxicity was identified by QSAR and luminous bacteria test.

2. Material and methods

2.1. Material

RDV (CAS number: 1,809,249-37-3), DEX (CAS number: 50-02-2) and HCQ (CAS number: 118-42-3) were purchased from Beyotime Biotechnology (RDV) and Shanghai Yuanue Bio-Technology respectively (DEX, HCQ). Acetonitrile and methanol were used in liquid chromatography (Simark, Germany). Ultrapure water was filtered by Synergy 185 water filtration system (Millipore, USA) to ensure resistivity greater than 18 MΩ cm.

2.2. Experimental procedures

The reference standards of the three target anti-COVID-19 drugs were dissolved into the ultrapure water and stirred to prepare stock solutions at a concentration of 10 mg/L. Then, they were diluted to 1 mg/L as the initial concentration of the experiment. The initial pH was adjusted to 5.0 and the drug-to-oxidant molar was set at 1:200. A 253.7-nm UV lamp with the intensity of 75 mW/cm² was placed above the reactor for a distance of 30 cm. A 100-mL sample was placed into a 250-mL reactor. The samples for degradation analysis were quenched by Na₂S₂O₃ (0.5 mol/L) and samples for toxicity analysis were quenched by bovine liver catalase (Sigma, 10 g/L).

Different experiments under reaction conditions, including the drug-to-oxidant molar ratio (1:200, 1:100 and 1:50) and pH (9.0, 7.0 and 5.0), were carried out to optimize degradation conditions for anti-COVID-19 drugs. After the degradation process, all the samples were filtered by 0.22-mm sterile filters (Millipore). The pH of the samples was adjusted by NaOH and H₂SO₄. The other reaction conditions were kept consistent during the reaction and each experiment was performed at least in triplicates.

2.3. Instrumentation and experimental conditions

The concentrations of the three anti-COVID-19 drugs were detected in positive ionization mode using the Shimadzu LC20ADXR HPLC system (Shimadzu, Japan) linked to an AB Sciex QTrap 5500 hybrid linear ion-trap triple quadrupole mass spectrometer (AB SCIEX, USA). The analysis method was optimized from the references (Dongre et al., 2009; Jin et al., 2017; Dadinaboyna et al., 2021). The software of Analyst 1.5.2. was used to acquire data. The chromatographic separation was performed on a C18 column (Agilent 5 HC-C18, 250 × 4.6 mm, 5 μm) and the instrument operating parameters and mobile phases were shown in Table S1–S3.

Besides, a LC20ADXR HPLC system (Shimadzu, Japan) connected to AB Sciex QTrap 5600 hybrid quadrupole-time-of-flight tandem mass spectrometry (LC-QTOF-MS) (AB SCIEX, USA) was used to confirm TPs. The transformation pathways and the main TPs of the three drugs were proposed based on LC-QTOF-MS detection and DFT calculation. In addition, total organic carbon (TOC) was measured with TOC analyzer (TOC-L, Shimadzu, Japan).
2.4. Computational methods

The possible active sites of three anti-COVID-19 drugs that were possible to be attacked by substances generated from the UV/AOPs system were predicted. The density functional theory (DFT) calculations and Fukui function values were calculated by the Gaussian 09 W and the details were listed in Table S5-S7. The DFT prediction combined with the TPs detected by LC-TOF-MS could help to analyze the degradation pathways and mechanism of anti-COVID-19 drugs in the UV/AOPs system.

The toxicity estimation software (T.E.S.T, version 5.1.1) provided by the US Environmental Protection Agency was employed to calculate the toxicity of RDV, DEX, HCQ and their TPs. The biotoxicity of the organics was simulated based on the quantitative structure activity relationship (QSAR) calculation model. Daphnia magna LC50, Ames mutagenicity and oral rat LD50 were chosen as the biotoxicity endpoints for QSAR prediction.

2.5. Luminescent bacterial test

Firstly, 10 mg/L of anti-COVID-19 drugs was degraded under UV/H2O2 conditions and the pH of samples was adjusted to between 5.0 and 8.0. The negative quality control was mixed by 1.0-mL ultrapure water and 0.1-mL 22% NaCl solution, and the positive quality control was mixed by 1.0-mL ultrapure water, 0.1-mL 22% NaCl solution and 10-μL ZnSO4·7H2O (100 mg/L). Then, the luminescent bacteria were incubated for 15 min at 4 °C. Afterwards, solution samples containing 3% NaCl were prepared by adding 0.1-mL bacterial suspension and 0.9-mL water samples. After 15 min, the luminescence values were measured by LUMIStox 300 (Hash, USA) and the relative bioluminescence inhibition rates (IR) were obtained by calculation.

3. Results and discussion

3.1. Degradation kinetics of UV and UV/AOPs

As shown in Fig. 1, the rate constants (k) of UV/H2O2 and UV were 0.02764 ± 0.00025 and 0.00615 ± 0.00020 s⁻¹ for RDV, 0.08168 ± 0.00194 and 0.03287 ± 0.00127 s⁻¹ for DEX and 0.03009 ± 0.00114 and 0.00578 ± 0.00017 s⁻¹ for HCQ, respectively. The degradation processes of three anti-COVID-19 drugs in ultrapure water were conformed to a pseudo-first-order kinetic model with a regression coefficient (R²) close to 0.99. The three anti-COVID-19 drugs almost had no decomposition (<1%) by adding H2O2 alone, meaning less effective during single oxidant conditions. Compared with UV irradiation alone, the degradation efficiency increased significantly under UV/H2O2 condition. The rate constants (k) ranking of UV/H2O2 was DEX > HCQ > RDV. DEX presented the highest degradation constant of UV/H2O2, which was similar to the previous study (Markic et al., 2018). With quenching by tert-butanol (TBA), HO• was verified to be essential for the degradation of RDV and HCQ under UV and UV/H2O2 process (Hu et al., 2022). UV excited HO• in the water to promote drugs degradation, and the addition of H2O2 elevated the HO• concentration to increase the efficiency (Rasolevandi et al., 2019a). However, DEX was decomposed by UV light without the involvement of HO• and the presence of HO• could further promote DEX degradation.

3.2. Effects of oxidant dosages on drugs decomposition

Usually, a high concentration of H2O2 indicated an increase in HO• content. As shown in Fig. 2, with the concentration of oxidant increased, the k (s⁻¹) increased from 0.01719 to 0.02762 for RDV and from 0.01234 to 0.03009 for HCQ. The increase in removal efficiency could
Fig. 2. The degradation kinetics of (a) RDV, (b) DEX, (c) HCQ, drug-to-oxidant molar ratio was 1:200, 1:100 and 1:50. Experimental conditions: the initial concentration of three pharmaceuticals was 1 mg/L; the initial pH was adjusted to 5.0.

Fig. 3. The degradation kinetics of (a) RDV, (b) DEX, (c) HCQ with the initial pH of 5.0, 7.0, 9.0 during UV/H$_2$O$_2$ process. Experimental conditions: the initial concentration of the three pharmaceuticals was 1 mg/L; the drug-to-oxidant molar ratio was 1:200.
be explained by the generation of HO· promoting the removal of anti-COVID-19 drugs by increasing the HO·

3.3. Effects of pH on drugs decomposition

The factor of pH usually have great effect on the concentration of HO· (Khylustova et al., 2016). The degradation kinetics of the three anti-COVID-19 drugs by UV/H2O2 process from pH 5.0 to 9.0 were shown in Fig. 3. The anti-COVID-19 degradation kinetics at alkaline pH conditions could be attributed to the reduced H2O2 decomposition to produce the reactive oxygen species (ROS) (Guo et al., 2021). The results revealed that the k constantly decreased with increasing pH. Among the three drugs, DEX was least affected by pH, which could be attributed to the higher UV photolysis efficiency reducing the influence of HO· in the UV/H2O2 process. Due to the higher output of HO· under acidic conditions, the highest k (s⁻¹) was obtained at pH 5.0, with 0.02764 ± 0.00024 s⁻¹ for RDV, 0.09137 ± 0.00253 s⁻¹ for DEX and 0.03009 ± 0.00114 s⁻¹ for HCQ. Interestingly, the kinetics of RDV in pH 9.0 was 0.01360 ± 0.00027 s⁻¹, which was close to 0.0146 ± 0.00014 s⁻¹ in pH 7.0, possibly owing to a certain degree of self-hydrolysis reaction occurring in alkaline and neutral conditions (Dadinaboyina et al., 2021). Previous studies also found the degradation promotion effect at a lower pH (da Silva et al., 2016; da Silva et al., 2021; Kargar et al., 2021; Pretali et al., 2021; Wla et al., 2021).

3.4. Mineralization of anti-COVID-19 drugs by UV/AOPs

Although UV/AOPs could degrade drugs to a lower concentration, it did not imply a high mineralization effect. For RDV, mineralization rates under UV/H2O2 were verified to be only 14.0% after 5 min (Fig. 4), while the mineralization rates of DEX and HCQ were much higher with the rates of 44.5% and 50.0% after UV/H2O2 treatment for 5 min. The mineralization rates were much lower than the excellent removal rates of the anti-COVID-19 drugs, indicating the presence of TPs.

A limited mineralization rate of RDV indicated that RDV was difficult to be degraded by hydroxy-radical oxidation process. As a nucleoside drug, RDV had more stable benzene-rings structures and nucleotide groups, which made it easy to remove but difficult to be completely mineralized (Hu et al., 2021). As shown in the DFT calculation results, RDV had more atoms with potential close to electric neutral with black and dark red in Fig. S1, which proved that RDV had more stable bonds and structures leading to mineralization barrier. Besides, more nitrogen-containing heterocyclic structures in the degradation products increased the stability of TPs (Yya et al.; Bejan and Damaeanu, 2020). As for DEX and HCQ, their rings were more easily opened to form TPs, such as carboxylic acids and aldehydes, which could further be mineralized easily. Previous studies also demonstrated that DEX and HCQ could eventually be converted into small molecule products (Rasolevandi et al., 2019a; Bensalah et al., 2020). In conclusion, when the action time of the UV/AOPs system was not sufficient, large amounts of TPs could be produced, which should arouse more attention.

3.5. Degradation pathways analysis by DFT and QTOF

The TPs and degradation pathways of the three anti-COVID-19 drugs were verified by DFT calculations and QTOF assays to reveal the structures and environmental risks of TPs. The TPs results were shown in Table 1. Figs. S1–S3 showed the charge distribution of optimized geometry molecule of the three anti-COVID-19 drugs. Fig. 5, S4 and S5 showed the proposed degradation pathways of these drugs. The TPs in brackets indicated their possible presence.

A proposed degradation mechanism of RDV degradation was shown in Fig. 5. As confirmed by DFT analysis, C26 was a favourable reactive site for electrophilic attack because of its largest atomic charge, meanwhile, HO· was easier to interact with C26 and generated RDV-TP620. Besides, RDV proceeded initial oxidation to form RDV-TP527, and then the relatively fragile chemical bonds O36–P13 and C20–C22 decomposed sequentially to form RDV-TP292 and RDV-TP265. Afterwards, RDV-TP174 was formed by the loss of C9H7NO2 and C9H7O2P groups.

As shown in Fig. S4, DEX was decomposed through three main

Table 1
The m/z, proposed chemical formula and retention time of transformation products.

| TPs                  | Retention time (min) | m/z     | Chemical formula       |
|----------------------|----------------------|---------|------------------------|
| RDV-TP619-1          | 25.48                | 602.2263| C27H26NO15P            |
| RDV-TP619-2          | 25.23                | 602.2492| C27H26NO15P            |
| RDV-TP619-3          | 21.39                | 620.0563| C27H26NO15P            |
| RDV-TP527            | 21.14                | 527.2007| C27H27NO14P            |
| RDV-TP402            | 28.88                | 402.1672| C27H27NO14P            |
| RDV-TP292            | 4.24                 | 292.2000| C27H27NO14P            |
| RDV-TP265            | 35.76                | 265.0984| C27H27NO14P            |
| RDV-TP174            | 20.19                | 174.1480| C9H7NO2               |
| DEX-TP424            | 38.23                | 425.2123| C9H7O2F               |
| DEX-TP409            | 23.77                | 409.2034| C9H7O2F               |
| DEX-TP391            | 28.98                | 391.2101| C9H7O2               |
| DEX-TP299            | 34.79                | 295.1624| C9H7O2               |
| DEX-TP273            | 34.67                | 273.1334| C9H7O2               |
| DEX-TP241            | 25.04                | 241.1430| C9H7O2               |
| DEX-TP227            | 14.33                | 227.0883| C9H7O2               |
| DEX-TP221            | 34.21                | 221.1182| C9H7O2               |
| HCQ-TP352-1          | 6.58                 | 352.2462| C9H7O2P               |
| HCQ-TP352-2          | 6.69                 | 352.2462| C9H7O2P               |
| HCQ-TP340            | 30.50                | 340.1613| C9H7O2P               |
| HCQ-TP308            | 31.82                | 308.2445| C9H7O2Cl              |
| HCQ-TP301            | 36.59                | 301.1414| C9H7O2O               |
| HCQ-TP179            | 8.91                 | 197.0382| C9H6NCl               |
| HCQ-TP176            | 28.11                | 176.1509| C9H2NO2               |
| HCQ-TP161            | 38.14                | 161.0579| C9H6O                  |
pathways. Because of the favourable reactive site of O6 according to DFT calculation, the first pathway was the hydroxyl substitution of aromatic rings, such as DEX-TP409 and DEX-TP424. In the second pathway, the side chain in the DEX molecule was broken due to the instability of the side chain between dihydroxyacetone and C11. Afterwards, the five-atom ring, carbon-fluorine and carbon-oxygen double bonds were attacked by the HO• to form DEX-TP299. In the last pathway, the bond of C10–F was replaced by C10–OH and the ring of carbon C10 was broken. Then, DEX-TP391 was attacked by HO• and formed DEX-TP227, DEX-TP241 and DEX-TP221. Finally, DEX-TP241 eventually transformed to DEX-TP273 by aldehyde reaction.

Fig. S5 showed that HCQ could be oxidized by HO• to form HCQ-TP352-1/2. Besides, HCQ was decomposed by breaking the chemical bonds of C12–N3, C23–Cl1 and C13–N4 to from aromatic and aliphatic TPs such as HCQ-TP308, HCQ-TP301, HCQ-TP176 and HCQ-TP179. After that, HCQ-TP308 and HCQ-TP179 were further oxidized by HO• to form HCQ-TP340 and HCQ-TP161.

3.6. Toxicity evolution on luminous bacteria during UV/AOPs treatment

Through mineralization and decomposition analysis, anti-COVID-19 drugs were found to have generated new TPs in the UV/AOPs process. Since the toxicity of these drugs and their TPs were unknown to the environment, it was essential to evaluate biotic toxicity to ensure technical safety. The toxicity evolution on the luminous bacteria test was shown in Fig. 6. RDV and HCQ showed a toxicity-increase region from 1 to 3 min for RDV and from 1 to 2 min for HCQ. The highest inhibition ratios of RDV on luminous bacteria were 36.4% at 2 min and 28.1% at 1 min, respectively. After 5-min reaction of the UV/H2O2 process, all the anti-COVID-19 drugs showed lower or similar luminescent bacteria toxicity than the initial values. The phenomena of rising rather than decline in toxicity during AOPs were also reported in other relevant studies (Hou et al., 2017; Zhu et al., 2021).

As shown in Table S4, except RDV-TP265, the toxicity of RDV and its TPs could not be predicted due to the lack of relevant QSAR data. However, in the luminous bacterial test (Fig. 7(a)), the maximum values of luminescence inhibition were found during the intensive production of TPs from 1 to 3 min. Thus, the identified TPs were inferred to be a potential bacterial toxicity contributor. Besides, the mixed toxicity of TPs might lead to increased product toxicity. Previous studies also found stacked toxicity of 2,3,4-THBP during the AOPs process (Zhang et al., 2021). The inhibition could also be attributed to the insufficient energy supply of ATP (Quiros et al., 2017). Due to the toxicity sensitivity of luminescent bacteria, biological toxicity not available in QSAR was found (Ma et al., 2014). Thus, this research complemented the lack of data on the environmental toxicity of RDV.

According to QSAR prediction in Table S4, most DEX and its TPs showed lower or similar initial biotoxicity than other drugs, meaning the degradation of DEX was a detoxification process. As shown in Fig. 7(b), luminous bacteria test verified this inference, the inhibition rate was gradually decreased as the production of TPs. Besides, the previous results presented that DEX among the three drugs had the highest degradation efficiency and higher mineralization rate, which lead to less TPs.
As shown in Fig. 7 (c), because of the simple structure of HCQ, several TPs were produced in the early stage of degradation and the toxicity-increase region occurred during this period. According to Table S4 and Fig. S4, when the N4–C8 bond was broken, the toxicity of HCQ-TP179 increased while toxicity of HCQ-TP176 decreased. Besides, the toxicity of HCQ-TP161 decreased from HCQ-TP176 after the replacement of the halogen atom Cl. Similarly, the toxicity of HCQ-TP301 decreased after the removal of Cl from HCQ. Therefore, the elevated toxicity of HCQ was mainly due to the halogen atoms Cl, which had a higher reactivity with proteins after halogenation (Kortagere et al., 2008). As increasing degradation time, the toxicity was reduced since Cl was replaced by HO•.

4. Conclusion

In this study, the degradation kinetics and optimal reaction conditions of three anti-COVID-19 drugs by the UV/AOPs were investigated. In ultrapure water, all the three anti-COVID-19 drugs could be degraded by more than 98% within 3 min and the optimal reaction conditions were pH of 5.0 with the drug-to-oxidant molar ratio of 1:200. Among the three drugs, DEX had the highest degradation efficiency with a rate constant ranking of DEX > HCQ > RDV, and only DEX was decomposed by UV photolysis without the involvement of HO•. By combining DFT and QTOF analysis, the degradation pathways and 24 TPs of three anti-COVID-19 drugs were proposed. The luminescent bacterial test showed a toxicity-increase region for RDV and HCQ, which agreed with the remarkable emergence of TPs. However, the luminescent bacterial toxicity of DEX gradually decline despite the emergence of TPs, which could be due to the higher mineralization rate of DEX and the low toxicity of TPs. Based on QSAR data, halogen group Cl mainly contributed to the toxicity of HCQ. In general, optimizing the reaction conditions and increasing the reaction time could ensure the removal efficiency and TPs biosafety of anti-COVID-19 drugs in the water body. At the same time, future studies should focus more on how to reduce the environmental hazard of TPs and ensure effluent biosafety under optimizing the cost of UV/AOPs technology.

Author contributions statement

Tenghao Huang: Data curation, Investigation, Formal analysis, Visualisation and Writing – original draft. Junjie Guo: Validation, Formal analysis and DFT calculations. Gang Lu: Conceptualisation, Methodology, Writing – review & editing, Supervision and Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

This study was financially supported by the National Natural Science Foundation of China (grant No.51508228), Guangdong Basic and Applied Basic Research Foundation (grant No. 2021A1515011804), Zhongshan Social Public Welfare and Basic Research Project (grant No. 210723154031576) and the Fundamental Research Funds for the Central Universities.

Appendix B. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.chemosphere.2022.134968.
Appendix A. Supplementary data

Supplementary data associated with this article can be found in the online version at.

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