

Degradation of iodinated X-ray contrast media by advanced oxidation processes: A literature review with a focus on degradation pathways

Meiru Hou^a, Xiaodie Li^a, Yu Fu^a, Lingli Wang^a, Dagang Lin^a, Zhaohui Wang^{a,b,c,*}

^a Shanghai Key Lab for Urban Ecological Processes and Eco-Restoration, School of Ecological and Environmental Sciences, East China Normal University, Shanghai 200241, China

^b Technology Innovation Center for Land Spatial Eco-restoration in Metropolitan Area, Ministry of Natural Resources, Shanghai 200062, China

^c Shanghai Engineering Research Center of Biotransformation of Organic Solid Waste, Shanghai 200241, China

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ABSTRACT

Available online Iodinated X-ray contrast media (ICMs) are clinical drugs used to enhance the imaging effect. Triiodobenzene ring structures of ICMs lead to its extremely high chemical stability, biological inertness, which makes it difficult to be completely removed by traditional water treatment processes. Hence, considerable concentration of ICMs can be frequently detected in aquatic environment. Relying on the strong oxidation capacity of HO[•] or SO₄^{•-}, various advanced oxidation processes (AOPs) have demonstrated substantial removal efficiency for ICMs. It is evident that ICMs can be decomposed mainly through (1) deiodination, (2) dehydration, (3) decarboxylation, (4) H-abstraction, (5) hydroxyl addition, (6) hydroxyl substitution, (7) oxidation of alcohol groups, (8) cleavage of amide bond, and (9) amino oxidation. However, during the ICMs removal process, the C-I bonds of ICMs molecules are broken, giving rise to the formation of cytotoxic iodination disinfection by-products (I-DBPs) that are potentially more harmful to the ecosystem and human health than their parent compounds. To better understand the technology gaps, this review elaborates the major AOPs which are effective for ICMs removal and emphasizes on the main degradation routes of ICMs in different oxidation system. Some prevailing concerns and challenges are discussed for optimizing the ICMs treatment process.

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1. Introduction

In recent years, the continuous accumulation of pharmaceutical compounds in the environment has attracted widespread attention. Iodinated X-ray contrast media (ICMs), 2,4,6-triiodine benzoic acid derivative, are an imaging-enhancing clinical pharmaceutical used in angiography, urography and computed tomography. To ensure the imaging contrast, ICMs are designed as inert and highly soluble drugs [1]. Due to their stable imaging performance and low toxicity to blood vessel wall and nerve tissues, ICMs have been extensively used. The application of iodinated contrast agents in angiography can be traced back to the 1920s [2]. In 2000, the annual consumption of ICMs exceeded 3500 tons, and Germany accounted for about 1/7 [3]. The iodine atoms attached to the aromatic ring of the contrast agent are responsible for absorbing X-rays and thus enhancing imaging [4], while the other polar groups are to ensure the high water solubility of ICMs and resis-

tance to human metabolism [5–7]. Moreover, the symmetric structure of 2,4,6-triiodine allows the high stability and biological inertness of ICMs. According to the position of polar carboxylic and hydroxy groups, ICMs can be roughly divided into ionic and nonionic agents [8,9]. Ionic agents with high osmotic pressure have free carboxylic moiety, while all carboxyl moieties of nonionic agents are amide derivatives and have low osmotic pressure [3]. Diatrizoate, iohexol, iopromide, iopamidol and iomeprol are common ICMs, and iopamidol has become the most frequently detected ICMs in aqueous environments [10]. The chemical structures of the five model compounds are shown in Fig. 1.

Since the last century, ICMs have been continuously developed and perfected in application, and until now contrast compounds exhibit extremely high chemical and biological stability to maintain their efficiency, as well as prevent undesired toxicological effects during the X-ray examination [11]. The chemical inertness of ICMs makes it difficult to be degraded, which can explain why residual ICMs and transformation products (TPs) were detected at µg/L level in the aqueous environment. Besides, high-dose use, continuous discharge and incomplete clearance account for the increasing ICMs concentrations in the environment. The

* Corresponding author.

E-mail address: zhwang@des.ecnu.edu.cn (Z. Wang).

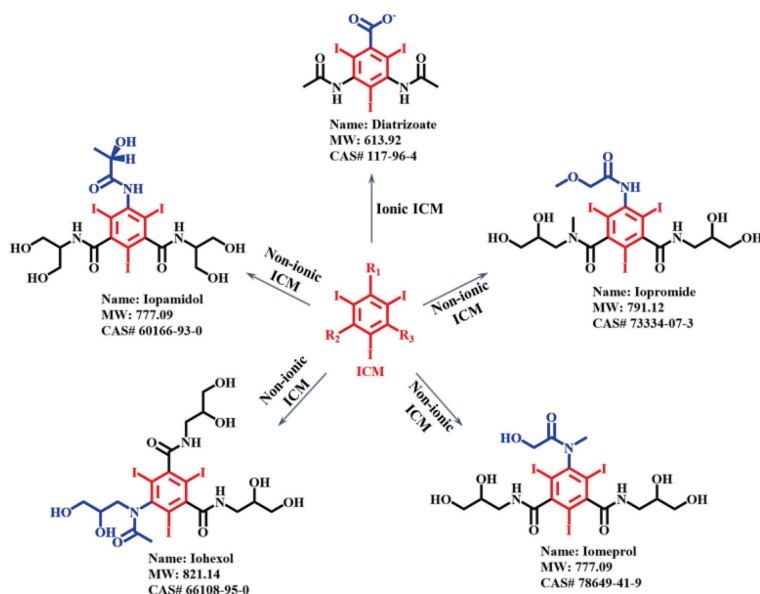


Fig. 1. The chemical structure of model ICMs.

earliest study on the effects of ICMs on aquatic organisms and human health can be traced back to the work by Steger-Hartmann *et al.* [12]. Short-term toxicity tests on bacteria, algae and fish with high ICMs concentration (10 g/L) showed no toxic effects of ICMs on the organism [12,13]. Nevertheless, it is found that iodinated components were major precursors for elevated absorbable organic iodine (AOI) concentrations of the hospital wastewater [14–16], but no direct evidence is available about the contribution of ICMs to high AOI concentration in aquatic environment [17]. Moreover, tri-iodo compounds are likely to produce iodinated disinfection by-products (I-DBPs). Decomposition of ICMs provides iodine atoms that react with organic matter in the process of drinking water disinfection to generate I-DBPs, which are more cytotoxic, genotoxic and ecotoxic than their chlorinated or brominated analogs [18,19]. ICMs concentration levels in the environment have been reported in the previous literature, but the data were scattered and not updated timely. This review has summarized the concentration values of ICMs in the aqueous environment of Asia, Europe and North America in the past two decades, which clearly illustrates that the pollution of ICMs is being aggravated. In order to minimize the potential adverse impact of ICMs on human health and ecosystem, it is urgent to remediate the contamination of ICMs. Many experimental results illustrate that advanced oxidation processes (AOPs) are the first choice to remove ICMs in the wastewater. In this review, AOPs for ICMs removal are divided into hydroxyl radical ($\text{HO}^\bullet$)-based AOPs and sulfate radical ($\text{SO}_4^{\bullet-}$)-based AOPs according to the types of radical oxidants. The oxidation mechanism and development of AOPs are also briefly summarized. Finally, this review makes a detailed classification and summary of the degradation pathways of different types (ionic and non-ionic) of ICMs in different oxidation systems, emphasizing the specific reactions of various radicals on certain functional groups of ICMs molecules. This review is expected to provide reference information for optimizing the removal technologies and also fill the knowledge gaps on ICMs degradation pathways.

2. ICMs contamination in the environment

ICMs are usually administered intravenously in high doses (200 g in a single dose, in which iodine content is approximately

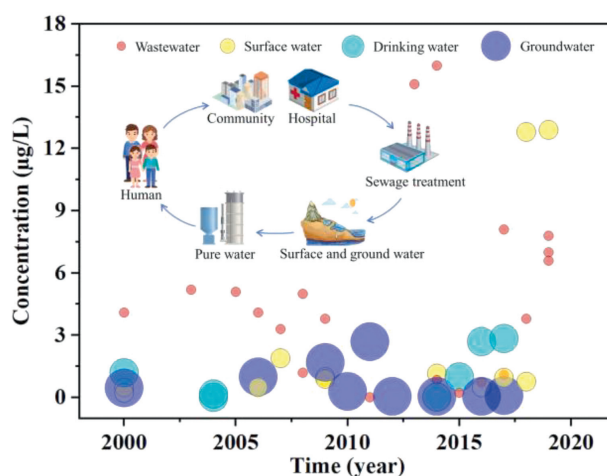


Fig. 2. The fate of ICMs in the aquatic environment and their concentration levels in various waters over the past two decades (2000–2022).

50%) [20]. The injected contrast agent is not metabolized and eventually excreted in urine or feces within 24 h. ICMs discharged from the human body flow into the Wastewater Treatment Plants (WWTPs) through the public sewage system. Recalcitrant properties (high stability, polarity and persistence) increase the difficulty in ICMs removal. Therefore, ICMs can exist for a long time after entering the water body through effluent discharge and sludge disposal [21], becoming one of emerging contaminants. The fate of ICMs in the aquatic environment and their concentration levels in various waters (wastewater, surface water, groundwater and drinking water) over the past two decades are shown in Fig. 2.

At the end of the 20th century, ICMs pollution levels in different environmental matrix were measured. X-ray contrast compounds were detected in drinking water [22], which was extracted from groundwater or river bank filtrate, but information on the behavior of ICMs during the passage of WWTP is missing [23]. During the decade of 2000 to 2010, more data on the ICMs concentrations level in the aqueous environment were reported. Ternes and Hirsch [3] monitored that ICMs load was significantly higher

on weekdays than that on weekends, because X-ray examinations were generally performed on weekdays in hospitals or clinics. In WWTPs, traditional water treatment processes are not designed to combat the resilient and persistent pharmaceutical compounds unless specifically designed to do so [24]. It is therefore understandable that appreciable concentrations of diatrizoate and iopromide (4.1 and 8.1 µg/L) was detected in the WWTP effluent, respectively [3,25]. After entering the receiving water, the ICMs concentration decreases continuously through physical actions such as dilution, filtration, and infiltration, and finally diffuses into groundwater or other surface waters. The concentration of ICMs was detected in groundwater in the range of 0.006–0.6 µg/L [26]. The mean values of ICMs concentration in receiving waters (rivers and creeks) were up to 0.49 µg/L for iopamidol and 0.23 µg/L for diatrizoate [3]. ICMs can still be detected in raw drinking water: 0.02 µg/L for iopromide, 0.17 µg/L for iopamidol, 0.03 µg/L for iohexol and 0.17 µg/L for diatrizoate, respectively [27]. This is because groundwater and surface water around cities can be used as drinking water sources for urban residents. However, data on the concentration of ICMs in groundwater are rather limited. Besides, the concentration level of ICMs depends on the usage dose and usage pattern. There are differences in the usage patterns of ICMs in different regions, and the ICMs concentration in wastewater are also different. Therefore, there is a lack of systematic studies on ICMs, such as concentration distribution, varying pattern. Since 2010, elevated concentration level in the aqueous environment have attracted widespread attention. Continued and excessive use of ICMs have resulted in the increased concentrations in natural waters (including surface water and groundwater), ranging from ng/L to mg/L [28–33]. The distribution of contrast compounds in surface water is wide and the geographical span is large, which makes it difficult to accurately detect the concentration of ICMs in various water bodies. According to the existing results, the occurrence of ICMs in different geographical divisions is summarized. In the surface waters of Asia, North America and Europe, the concentration ranges of ICMs are 0.001–7.8 µg/L [34–37], 0.02–0.16 µg/L [38] and 0.01–7 µg/L [39–42], respectively. Compared with that in the period of 2000–2010, the increasing trend of ICMs content in the surface water is evident. Data on ICMs contamination in groundwater are always scarce because of sampling difficulty. Generally, the interception and filtration of soil particles makes the content of ICMs entering the groundwater very low. The mean ICMs concentration value in groundwater was 0.003 µg/L in 2011 [43], with an increase of 0.06 µg/L over the next five years [44,45], and increasing to 0.1 µg/L in 2017 [46]. It can still be inferred that the content of ICMs increases yearly. ICMs persisted in various drinking water treatment processes, and eventually trace amounts of ICMs were detected in drinking water. In the effluents of drinking water treatment plants in Asia, North America and Europe, concentration of ICMs ranged 0.001–1.6 µg/L [47,48], 0.01–2.7 µg/L [10], and 0.001–0.5 µg/L [49,50], respectively. The highest concentration value in drinking water is around 10-fold higher than that in the opening decade of the 21st century [27].

In the past 20 years, ICMs have received considerable attention, but data on their pollution levels are mostly scattered. Long-term (different period, same area) and large-scale (same period, different area) survey on ICMs contamination are lacking. In addition, ICMs content in some areas is lower than the quantitative detection limit of existing methods, resulting in the difficulty of the precise concentration detected in the environment. The upward contamination trend has drawn attention to the threat of ICMs to the health and life of non-target organisms. According to the precautionary principle, contrast media should be removed from the environment whenever possible to minimize the risk of unpredictable long-term effects.

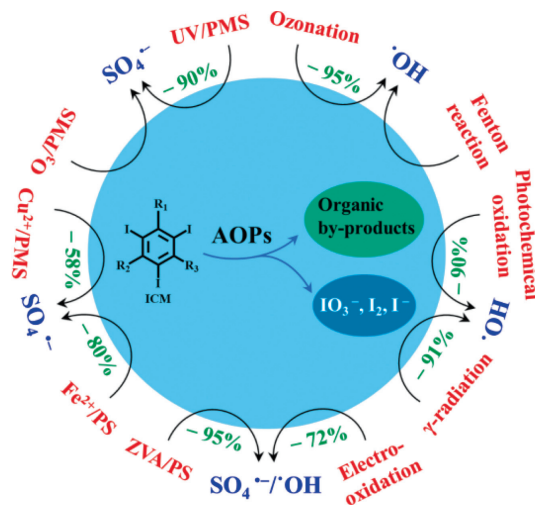


Fig. 3. AOPs for ICMs removal. Blue, red and green denote the main radical species, the specific AOPs, and the removal rate of AOPs for ICMs, respectively.

3. AOPs as removal technologies for ICMs

AOPs have advantages over phase transfer techniques because AOPs can destruct contaminants compared to physical removal. Unlike chemical oxidation, AOPs transform contaminants into stable, low- or nontoxic species by generating highly reactive free radicals at ambient temperature and pressure, which is suitable for achieving the complete abatement and mineralization of the contaminants [51–53]. Active free radical species are atoms or molecules containing at least one unpaired electron, such as the superoxide anion radical ($O_2^{\cdot-}$), hydroperoxyl radical ($HO_2^{\cdot}$), alkoxy radical ($RO^{\cdot}$), $HO^{\cdot}$ and $SO_4^{\cdot-}$ [24]. AOPs have shown outstanding performance for removal of contrast agents in wastewater, which is mainly attributed to the strong erosion of ICMs by $HO^{\cdot}$ and $SO_4^{\cdot-}$, and organic by-products and iodine-containing compounds are the main degradation products. Fig. 3 summarizes the major AOPs and their general treatment efficiency for ICMs by applying various oxidants.

3.1. $HO^{\cdot}$ -based AOPs

$HO^{\cdot}$ is an important reactive radical in various AOPs due to its powerful oxidizing capabilities ($E_0 = +2.80$ V vs. NHE), non-selectivity and high reactivity. Generally, $HO^{\cdot}$ reacts with organic compounds through electron transfer, $HO^{\cdot}$ addition or H-abstraction [54]. Fenton reaction, γ -radiation and electrooxidation reaction are typical $HO^{\cdot}$ mediated AOPs. While the efficiency of single AOP is limited, the integration of multiple AOPs can synergistically accelerate the degradation rates, such as UV/ O_3 , electrochemical/biological treatment.

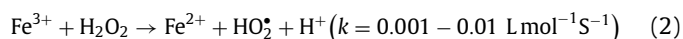
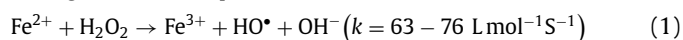
3.1.1. Ozone oxidation

Ozone (O_3) reacts with specific functional groups of contrast agent contaminants, especially aromatic and unsaturated moieties, degrading pollutants into low-molecular weight substances [55–57]. With the increase of O_3 dosage and concentration, the ozonation efficiency of ICMs will also increase [52,58–60]. At the O_3 concentration of 1 mg/L and the maximum 15 mg/L, the removal rates of ICMs were below 20% and about 70%, respectively [52,61]. However, the removal rate is not infinite and also leads to cost increase. In addition, adding catalyst (e.g., metal ion or ion catalyst) or combined with other processes (e.g., O_3/H_2O_2 and O_3/UV) increases the production of $HO^{\cdot}$, which is more oxidative to contrast media than O_3 alone [58,62–65]. Ternes *et al.* found that adding

H₂O₂ (10 mg/L) before ozonation (10 mg/L) increased the oxidation efficiency of ICMs from 40% to 57%–85% [52]. Under the action of light, light energy accelerates the destruction of O₃ and makes the decomposition of organic pollutants faster and more complete. Therefore, O₃/UV can also minimize the contaminants load of pharmaceuticals discharged into aquatic environment [63]. The removal rates of the non-ionic ICMs in O₃/UV and O₃/UV/H₂O₂ were more than 95%, higher than that in O₃/H₂O₂ (about 50%), and is much higher than that of O₃ alone ($\leq 30\%$) [51]. Moreover, the combination of O₃ and sonication has been applied in reducing membrane fouling, but it has not been applied in destroying the ICMs in the environment. At present, there is little information on the degradation of contrast agents by O₃ catalysis, especially the information on degradation products and toxicity evaluation, which needs to be further explored.

3.1.2. Fenton reaction

Fenton reagents (H₂O₂ and Fe²⁺) rapidly generate HO• that decompose ICMs via the following reactions (Eqs. 1 and 2) [66], resulting in the decomposition of ICMs.



Modified Fenton reaction (classified as “Fenton-like” reactions, such as “photo-Fenton” process, “electro-Fenton” process and “sono-Fenton” process and their combinations) [67] and a series of iron-free Fenton reactions (catalysts such as Al, Co, Cr, Cu, Mn, Ru and Ce) [66] can overcome the strict acidic condition of traditional Fenton reactions and have good degradation effects on ICMs. In the conventional Fenton reaction, approximately 22.4% of diatrizoate was mineralized [68]. Photo-assisted Fenton can further improve the removal rates of contrast media [69], up to 64.7% [70]. About 72% of diatrizoate can be removed at the H₂O₂ concentration of 50 mg/L [68]. Coupling photo-Fenton with electro-Fenton can achieve complete mineralization of diatrizoate [71]. The photo/ferrioxalate reaction system is also an effective way to expand the pH range of the traditional Fenton reaction [72]. Under UV-visible light irradiation, the oxygen-containing reactive species (e.g., H₂O₂ and HO•) can be generated through the reaction of Fe³⁺/Fe²⁺-oxalate complexes, leading to the degradation of organic pollutants [69,73–75]. In the Fe³⁺-oxalate/H₂O₂ photochemical system, 95% of iopamidol was removed. In addition, non-metallic catalysts (elements with multiple redox states) can achieve *in situ* generation of HO• and decomposition of H₂O₂ through an electron transfer process, which can also broaden the pH range of the Fenton reaction [66].

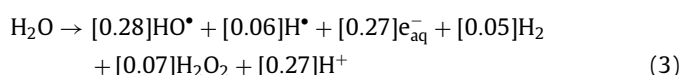
3.1.3. Photochemical oxidation

Contrast agents can remove organically bound iodine to form intermediates by direct photolysis under simulated sunlight, or indirectly by free radicals generated in solution. Under solar UV radiation, the photons are absorbed by organic molecules, resulting in excitation of molecules, forming active free radicals that contribute to the elimination of contaminants in the environment [76–78]. The degradation rates of diatrizoate and iohexol in UV irradiation were 30% and 27%, respectively. In Titanium dioxide (TiO₂) suspension after UV irradiation, diatrizoate and iohexol can adsorb HO• and release the iodine species, resulting in partial diatrizoate decomposition (40% and 38%, respectively) [79,80]. In review of the significant radiation energy loss in the electron-hole recombination process in the UV/TiO₂ system, an alternative electron acceptor (H₂O₂) can be used to capture electrons and suppress the recombination effect [81–83]. Moreover, adding H₂O₂ is beneficial to accelerate the degradation reaction of ICMs [84–88]. Due to the limited removal capacity of single photochemical reaction, only partial

mineralization occurs with photochemical oxidation alone [89,90]. Upon coupling photochemical with biological treatment, 90% of the diatrizoate or iohexol can be removed [91]. The combination of UV and chlorine (UV/HOCl or UV/ClO₂) can also remove ICMs [92]. Chlorine treatment alone resulted in less than 10% removal of iopamidol, compared to over 90% in UV/chlorine [93]. The removal rate of diatrizoate by direct photolysis was 12.8%, and that reached 85.9% after adding reactive chlorine species [94]. It can both alleviate the energy consumption and reduce the treatment costs. Yet UV irradiation increases the risk of I-DBPs formation, therefore, it is necessary to optimize the oxidation process to avoid the formation of I-DBPs and prevent secondary pollution.

3.1.4. γ -radiation

Gamma radiation (γ -radiation) generates various highly active free radical species, including oxidizing species (HO•, H₂O₂ and O₂) and reducing species (H• and e_{aq}[−]) by reacting with or destroying water molecules (Eq. 3) [95,96], which can oxidize the functional groups on the side chains of ICMs to achieve their degradation.



γ -radiation interacts with carboxyl or phenolic groups, changing the properties of the parent compound and enhancing its degradability [97,98]. Jeong *et al.* [99] found that 68%–79% of the non-ionic ICMs (iohexol) and 40% of the ionic ICMs (diatrizoate) were removed by onizing irradiation, while the iodine released from diatrizoate and iohexol were 88% and 99% of total iodine in molecules, respectively. Velo-Gala *et al.* [100] found the maximum removal rate of diatrizoate was up to 91.9% (initial concentration of 25 mg/L). Compared with γ -radiation alone, the joint process can accelerate the reaction and complete the sewage purification in shorter time. But the efficiency of γ -radiation is still limited. If an appropriate electron accelerator is used in the application process, thousands of cubic meters of wastewater can be treated every day [101]. Besides, γ -radiation can simultaneously and quantitatively generate all three reactive species found in all AOPs at concentrations ranging from nmol/L to mmol/L [102], which is one of the advantages of AOPs for contaminants removal. It represents a new and efficient method for abatement of ICMs. However, there are only few cases on ICMs removal by γ -radiation, and further investigations on its applicability to other ICMs are needed.

3.1.5. Electrochemical oxidation

Electrochemical processes show significant advantages in eliminating ICMs. During the electrochemical treatment, ICMs are oxidized by HO• at the anode, similar to the oxidation mechanism of other AOPs. It does not add chemical reagents and operates at ambient temperature and pressure. Most importantly, no waste stream is generated during the electrochemical process [103–106]. Diatrizoate and iopromide have different efficiencies in various anodic solutions, for example, 86% and 79% for diatrizoate, $\leq 75\%$ and $\leq 46\%$ for iopromide in nitrate and sulfate anolyte, respectively [106–108]. ICMs degradation rates were more than 85% when perchlorate was used as the electrolyte [109]. The electron transfer to the ICMs molecules causes its destabilization and decay into separate fragments [110]. Electrochemical treatment affects the biodegradability by altering the specific functional groups of ICMs, which usually makes the biodegradability of the degradation products higher than that of the ICMs parent compounds [111]. The coupling of electrochemistry and biodegradation (Membrane Bioreactor/Moving Bed Bioreactor, MBR/MBBR) enables C-I bond cleavage to form the organic by-products and iodine-containing species, where ICMs degradation by-products are used as carbon sources and are further mineralized during the subsequent biological treatment [112,113]. In addition, the high energy cost of electrochemical

process is acceptable to a certain extent, as this can improve the cost performance of electrochemical treatment by developing novel electrode materials and optimizing cell parameters [109]. Nevertheless, the coupling of electrochemical and biological process is currently only used in the laboratory without any practical application cases [114].

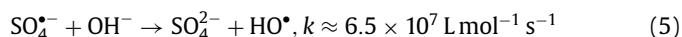
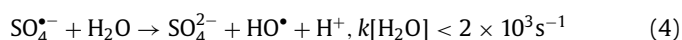
3.2. $\text{SO}_4^{\cdot-}$ -based AOPs

$\text{SO}_4^{\cdot-}$ is a highly aggressive oxidant in water because of its high redox potential and long lifetime. Compared with $\text{HO}^\bullet$, reactions between organic contaminants and $\text{SO}_4^{\cdot-}$ are selectively and less affected by natural organic matter (NOM) or solution pH. $\text{SO}_4^{\cdot-}$ reacts with organic components mainly *via* electron transfer, and finally selectively mineralizes the organic components into low-toxic or nontoxic substances. $\text{SO}_4^{\cdot-}$ could be produced through heat, base, transition metal ions (*i.e.*, Co^{2+} , Cu^{2+} and Fe^{2+}) and UV-light decomposition of the precursors of $\text{SO}_4^{\cdot-}$, such as persulfate (PS) (including peroxymonosulfate (PMS) and peroxydisulfate (PDS)) and sulfite [115–118]. Using $\text{SO}_4^{\cdot-}$ to remove pharmaceutical compounds has received widespread attention, including ICMs.

Copper ions (Cu^{2+}), cobalt ions (Co^{2+}) and iron ions (Fe^{2+} or Fe^{3+}) are the common transition metal ions used to activate sulfate to produce $\text{SO}_4^{\cdot-}$. Co^{2+} mediated activation of sulfate including PDS [116] and PMS [119] show optimistic results for the removal of the target compounds. In the Co^{2+} /PMS system, $\text{SO}_4^{\cdot-}$ oxidized ICMs (iomeprol and iohexol) to organic by-products and iodate (IO_3^-), with a high removal rate but a low mineralization. In addition, iohexol is more stable than iomeprol and is more difficult to be decomposed by $\text{SO}_4^{\cdot-}$ [119]. Cu^{2+} / Co^{2+} activated sulfite autooxidation is a chain reaction. Generation of oxy-sulfur radicals excited by direct single electron transfer from hexavalent sulfur to Cu^{2+} / Co^{2+} to degrade contrast agents [120,121]. Introducing iron ions into reaction of $\text{SO}_4^{\cdot-}$ and ICMs, the removal of target compounds will be significantly enhanced. The use of PMS alone can remove 21% of ICMs, the removal rate of ICMs in Cu/PMS system was doubled, and the addition of Fe^{3+} in Cu/PMS system can increase ICMs removal rate from 42% to 58% [107]. The removal effect of iron-activated sulfite to generate $\text{SO}_4^{\cdot-}$ for ICMs is not inferior to that of Cu/sulfite or Co/sulfite. In the Fe/PS system, approximately 80% of non-ionic ICMs can be degraded and about 69% of ionic ICMs can be removed, which cannot be achieved by using ferrous or PS alone [122–124]. The participation of H_2O_2 in Fe/PS system promoted Fe^{3+} reduction and PS decomposition to accelerate the degradation of ICMs [118]. Fe/PS exhibited a good efficiency for decontamination of ICMs, along with low cost and good performance, making it a promising alternative to conventional AOPs. However, the complex reactive species and transformation mechanisms remain elusive [125]. Except for transition metals (Co^{2+} , Cu^{2+} and Fe^{2+}), zero-valent aluminum (ZVA) can also activate PS (ZVA/PS) to promote the generation of $\text{SO}_4^{\cdot-}$, much better than $\text{ZVA/H}_2\text{O}_2$. ZVA/PS removed 95% of ICMs in distilled water, while the removal rate of ICMs in $\text{ZVA/H}_2\text{O}_2$ was less than half of that in ZVA/PS . Although ZVA/PS can only remove 29% of ICMs in surface water, the removal rate of ICMs in $\text{ZVA/H}_2\text{O}_2$ was still less than half of that in ZVA/PS [1]. Photo-activated PDS is one of the extensively used $\text{SO}_4^{\cdot-}$ -based technologies other than transition metal ions. In UV irradiation and PDS system (UV/PDS), 90% of ICMs can be destroyed by direct photolysis, direct oxidation *via* PDS, or $\text{SO}_4^{\cdot-}$ attack [126,127]. ICMs were oxidized by $\text{SO}_4^{\cdot-}$ to generate intermediates and then mineralized into carbon dioxide (CO_2) and water (H_2O) through UV irradiation [128]. However, there is a lack of relevant information on the mechanism and kinetics of ICMs removal by $\text{SO}_4^{\cdot-}$. The UV- Fe^{3+} -sulfite oxidation process, based on Fe^{3+} catalyzed sulfite oxidation and photochemistry of Fe^{3+} species, is a new facile route for the generation of

$\text{SO}_4^{\cdot-}$ [129]. However, there is no experimental data for ICMs removal. In addition, sulfate-mediated electrooxidation is also an alternative method to remove more than 50% of the contrast agent in the solution. Sulfate solution acts as a supporting electrolyte for the anodization of pollutants, which facilitates the formation of intermediates ($\text{SO}_4^{\cdot-}$) at boron-doped diamond (BDD) anodes and enhances the decontamination ability of the solution. In the sulfate anolyte, the deiodination efficiency of diatrizoate was around 80%, compared with that of iopromide is less than 46% [108].

In some reactions, the synergetic effect of $\text{HO}^\bullet$ and $\text{SO}_4^{\cdot-}$ contributes to the abatement of pollutants. For instance, coupling O_3 with PMS (O_3/PMS) can simultaneously generate two free radicals, $\text{HO}^\bullet$ and $\text{SO}_4^{\cdot-}$, which can not only accelerate the degradation of ICMs, but also decrease greatly the concentration of formed I-DBPs [130,131], offering a new option for the effective abatement of recalcitrant contrast media. Moreover, the generated free radicals through the decomposition of PS in strongly alkaline ($\text{pH} > 11$) solution is mainly $\text{HO}^\bullet$, and is $\text{SO}_4^{\cdot-}$ in the solution with $\text{pH} < 9$ [115]. In addition, sulfate radical can also yield $\text{HO}^\bullet$ under neutral or basic conditions (Eqs. 4 and 5) [132,133].



Although $\text{SO}_4^{\cdot-}$ -based AOPs seem promising for removing ICMs in water, the key problem is its low mineralization rates to ICMs molecules. More importantly, there is no systematic information available in literature related to the abatement of ICMs, such as the identity of produced complicated reactive species. In addition, the transformation kinetics and mechanism are still not confirmed, which need to continue to explore.

4. Degradation pathways of common ICMs

The high degradation/low mineralization rates indicate that the degradation of ICMs is not caused by the complete destruction of the entire ICMs molecules. This also explains why the TPs in the ICMs degradation contain a complete benzene ring and some specific polar groups. The degradation products were analyzed by high performance liquid chromatography/tandem mass spectrometry (HPLC/MS), and the degradation pathways of ICMs in different AOPs system were speculated. The side chain intermediates of different ICM in the same oxidation system or the same ICM in different oxidation systems varied slightly. According to the identification and analysis of the transformation products, the degradation pathways of ICMs mainly include deiodination, dehydration, decarboxylation, H-abstraction, $\text{HO}^\bullet$ addition, $\text{HO}^\bullet$ substitution, oxidation of alcohol groups, cleavage of amide bond and amino oxidation. The degradation pathways of ICMs largely depend on the chemical structures of ICMs and the treatment technology. For example, decarboxylation is one of the important degradation routes for ionic ICMs with polar carboxyl groups (diatrizoate), and generally does not happen in the decomposition processes of non-ionic ICMs (iopamidol, iomeprol, iohexol and iopromide). However, not all transformation products can be detected. For instance, products of iopromide from C-I bond cleavage in electrooxidation may have been rapidly converted into (poly) hydroxylated and aliphatic products, which will be more difficult to be detected by HPLC/MS [108]. Therefore, based on previous studies and most of the identified by-products, this review can only tentatively propose some general pathways of ICMs (Figs. 4–6).

Deiodination is one of the major routes for the decomposition of all triiodide compounds (both ionic and non-ionic) [134]. The carbon atoms connecting the I atom are all positively charged in the ICMs molecules, while the three I atoms are negatively

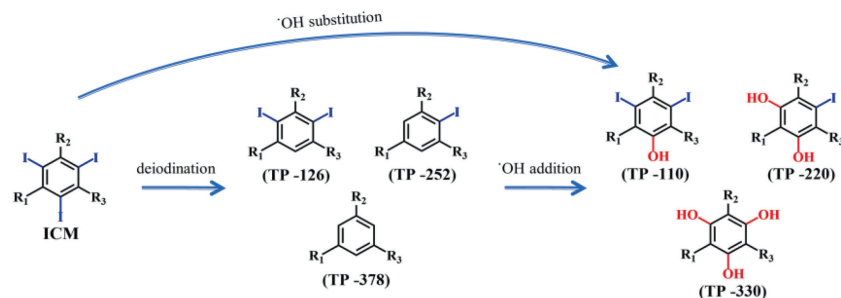


Fig. 4. The proposed pathways of deiodination from ICMs by AOPs.

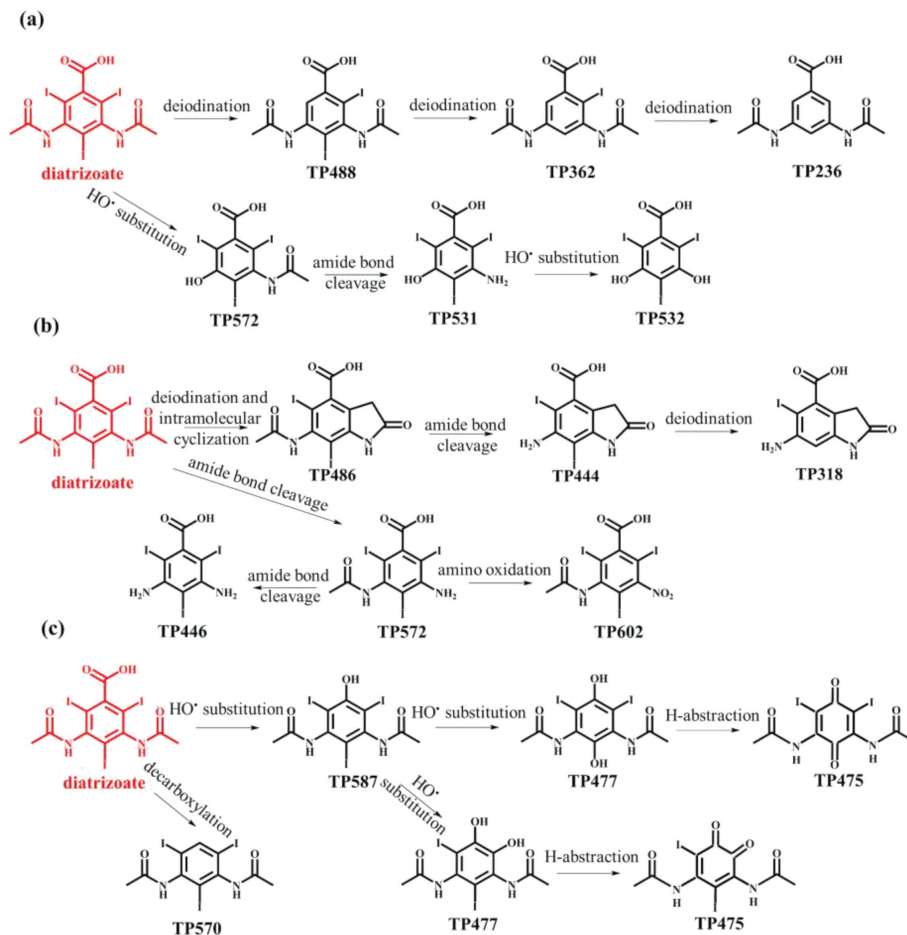


Fig. 5. The specific degradation pathways of ionic ICMs in (a) $\text{HO}^\bullet$ mediated oxidation system, (b) $\text{SO}_4^{\bullet-}$ mediated oxidation system and (c) common pathways in typical AOPs.

charged. Due to the different steric hindrance effects of the substituents on the side chain of the benzene ring, the charge density on the C atom is also slightly different. The C atom with the largest negative atomic charge is more susceptible to electrophilic attack by $\text{HO}^\bullet/\text{SO}_4^{\bullet-}$ to achieve the decomposition of ICMs molecules [119]. By detecting the concentration of iodine atoms in the solution, it is found that with the prolongation of the reaction time, the released iodine atom increased continuously, implying that the tri-iodine contrast agent was gradually de-iodized. The process of iodine removal from ICMs is described in Fig. 4.

The C-I bond is cleaved to release the iodine atom from the benzene ring and form deiodinated products, followed by $\text{HO}^\bullet$ addition to the iodine site to form phenolic products. The iodine atom attached to the benzene ring also can be directly substituted by $\text{HO}^\bullet$ and form the phenolic products. After deiodination of ICMs,

the iodine atoms are released from the benzene ring into the environment, some of them will combine with the organic matters in the environment to generate IO_3^- , and the remaining will become the source of I for the formation of I-DBPs. Since the ICMs molecules contain a benzene ring, symmetrical alkyl side chains and three iodine atoms attached to the 2, 4, 6 position on the benzene ring, indistinguishable isomers are generated during the degradation process. In order to simplify the description of the ICMs degradation processes, only one structure of multiple isomers is provided in the ICMs degradation pathways diagram.

4.1. Ionic ICMs

Triiodo-benzoic acid (diatrizoate) is a typical ionic ICM with free carboxyl groups and amide groups in the side chain.

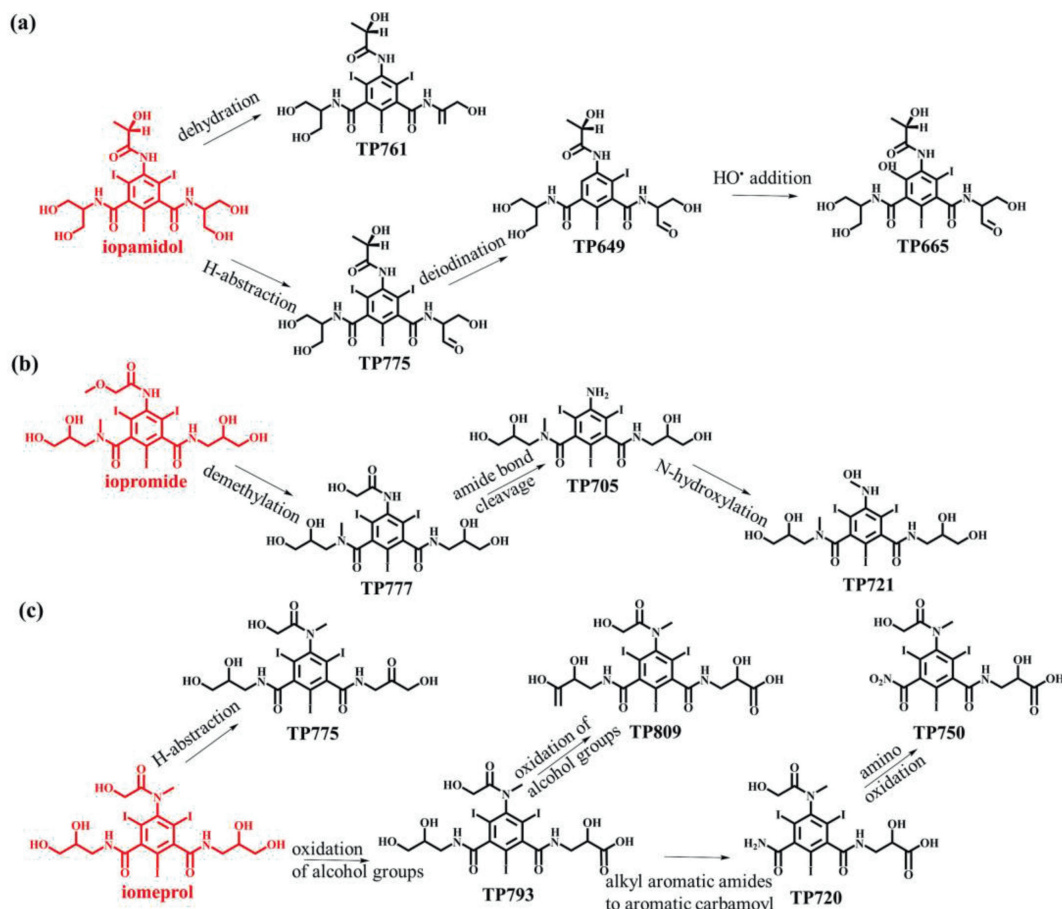


Fig. 6. The specific degradation pathways of non-ionic ICMs in (a) $\text{HO}^\bullet$ mediated oxidation system, (b) $\text{SO}_4^{\bullet-}$ mediated oxidation system and (c) common pathways in typical AOPs.

γ -radiation, electro-oxidation and sunlight-activated PS processes are effective for removal of diatrizoic acid, which are attributed to the oxidation of free radicals ($\text{SO}_4^{\bullet-}$ or $\text{HO}^\bullet$) [100,109,127]. The main oxidant produced by γ -radiation is $\text{HO}^\bullet$, while in the electro-oxidation system (in Na_2SO_4 anolyte) and simulated sunlight-activated PS system, the main oxidant is $\text{SO}_4^{\bullet-}$. Some specific structures in the diatrizoate side chain were selectively destroyed by $\text{SO}_4^{\bullet-}$ different from the non-selective decomposition of ICMs by $\text{HO}^\bullet$. Fig. 5 shows the main degradation pathways of ionic ICMs degradation.

As shown in route (a), under the exposure to $\text{HO}^\bullet$, the ionic ICMs are gradually deiodinated to form incomplete and complete deiodination products (TP488, TP362 and TP236). Moreover, in the $\text{HO}^\bullet$ -mediated oxidation system, $\text{HO}^\bullet$ substitution and $\text{HO}^\bullet$ addition seem to be a common degradation pathway. This was also confirmed by the formation of a large number of phenolic intermediates during ICMs decomposition (TP572, TP531 and TP532). The pathways of $\text{SO}_4^{\bullet-}$ -mediated degradation of ionic ICMs are shown in route (b). After breaking C-I bond on the benzene ring, the adjacent alkyl side chain undergoes intramolecular cyclization to form the intermediate TP486. An intermediate similar to TP486 was also found in the photocatalytic degradation of diatrizoate by TiO_2 [135]. Under the continuous oxidation, the amide bond of the side chain of TP486 is cleaved to form the aniline derivative TP444, and the C-I bond is directly cleaved to form the degradation product TP318. The amide bond connected to the benzene ring in diatrizoate molecule is broken to form TP572, and the newly formed amino group is further oxidized to nitro group to form the nitro derivative TP602 or its symmetrical amide bond are

destroyed to form symmetrical TP446. This degradation route occurs in the degradation process of almost all the ICMs containing amide bonds. It is speculated that the initial step in the reaction of $\text{SO}_4^{\bullet-}$ with diatrizoate is the electron transfer from diatrizoate to $\text{SO}_4^{\bullet-}$ and the generation of radical cations, and corresponding HO-adducts is generated by hydrolysis. Route (c) is the overlapping part of the ICMs degradation pathways in the $\text{SO}_4^{\bullet-}$ and $\text{HO}^\bullet$ system. The decarboxylation process is similar to deiodination process. The simplest decarboxylation is that carboxyl group ($-\text{COOH}$) is directly detached from the benzene ring to form decarboxylation product TP570. $\text{HO}^\bullet$ is added to the carboxyl site and replaces $-\text{COOH}$ or the addition of $\text{HO}^\bullet$ of the decarboxylation product can also achieve decarboxylation. The addition of $\text{HO}^\bullet$ to the carbon site connecting the carboxyl group will cause decarboxylation and hydroxylation to form the intermediate TP586, and the addition of $\text{HO}^\bullet$ to the iodine site will cause diiodine hydroxylation to form the hydroquinone product TP476 and the quinone product TP474. The order of deiodination and decarboxylation cannot affect the degradation rates of diatrizoate. Hydroquinone and catechol, paraquinone and orthoquinone products are isomers of each other, with the same formation mechanism. This degradation process has been confirmed in previous report by Zhou et al. [128]. In addition, according to the change of absorbance with reaction time during the reaction between $\text{SO}_4^{\bullet-}$ and diatrizoic acid (rising first and then falling), it is inferred that the reaction of $\text{SO}_4^{\bullet-}$ and diatrizoate is only the first step of the whole reaction, and the intermediate will continue to be oxidized after absorbing sunlight or visible-light. For example, the conversion of hydroquinone product to quinone product seems more

like a photodegradation pathway than a $\text{SO}_4^{\cdot-}$ oxidation process [128].

4.2. Non-ionic ICMs

The degradation pathways of non-ionic ICMs are much complicated. Except for the conventional deiodination, H-abstraction, $\text{HO}^\bullet$ substitution and $\text{HO}^\bullet$ addition, there are also dehydration, demethylation, and oxidation of alcohol groups (to form aldehyde groups, ketone groups, and carboxyl groups), cleavage of amide bond, amino hydrolysis (or amino oxidation) and other typical decomposition paths. Taking the degradation of iopromide in electro-oxidation (sulfate anolyte) system [108], the decomposition of iopamidol under UV irradiation [99,134], and the oxidation of iomeprol by reactive oxide species ($\text{SO}_4^{\cdot-}$ and $\text{HO}^\bullet$) [99,119] as examples, the typical degradation pathways of non-ionic ICMs in AOPs are illustrated in Fig. 6.

The non-ionic monomeric contrast agent iopamidol, first launched in Italy in 1981, is the most frequently detected ICM in aqueous environments [10]. The destruction routes of iopamidol during UV exposure are shown in route (a). Upon UV radiation, iopamidol directly adsorbs photons and degrades into more degradable intermediates. Hydrogen is extracted (H-abstraction) from the primary alcohol group of alkyl side chain to form the aldehyde product **TP775**. Seitz *et al.* proposed three structures for **TP775**, including two types of aldehydes and ketones, and confirmed the appearance of aldehyde and carbonyl functional groups in the main product of iomeprol during ozonation [67], according to the derivatization method [119]. The formation of the aldehyde functional group in the product **TP775** results from the oxidation of aliphatic alcohols. Observation of carboxyl groups in some other intermediates of ICMs confirmed the existence and rationality of this type of the loss of 2 mass units [119]. In the subsequent oxidation reaction, the C-I bond is broken to form the deiodinated product **TP649**, and $\text{HO}^\bullet$ is added to the site of the removed I to form phenolic products **TP665**. Another way of the formation of **TP665** is that the iodine atoms on iopamidol can be directly substituted by $\text{HO}^\bullet$. In Fe^{3+} -oxalate/ H_2O_2 /photochemical system, iopamidol reacts with $\text{HO}^\bullet$ and decomposes through oxidation processes such as deiodination, H-abstraction, $\text{HO}^\bullet$ addition and $\text{HO}^\bullet$ substitution. This is similar to the destruction pathways of iopamidol in the UV irradiation system. The side chain of iopamidol can be dehydrated to form the dehydration product **TP761**. Furthermore, the decomposition process of iopamidol in the photochemical reaction appears to be initiated by the carbon dioxide anion radicals ($\text{CO}_2^{\cdot-}$) in the absence of oxygen. $\text{CO}_2^{\cdot-}$ (a powerful reducing agent) can reduce the aromatic ring of iopamidol to produce free radical anions. Subsequent elimination of iodine atoms and H-abstraction to produces by-products. The reduction degradation routes have been reported, for example, iomeprol under high energy pulse and γ -radiolysis [99], and iopamidol under photochemical treatment [75].

Iopromide (the brand name Ultravist in Europe and the United States) was introduced to the German market in 1985. In the Co/PMS system, $\text{SO}_4^{\cdot-}$ plays a major role in the iopromide removal. Iopromide is completely deiodized during electrooxidation, which takes place in single-chamber electrolysis cell, so that cathodic deiodination occurs simultaneously with anodic oxidation [113]. The most distinctive products in the degradation process are **TP777** (demethylation product of alkyl side chain) and **TP721** (the product of amide bond cleavage and N-hydroxylation). The formation of demethylation product **TP777** is attributed to the O-demethylation of the iopromide side chain, which is initiated by the H-abstraction by $\text{SO}_4^{\cdot-}$ and the formation of carbon-centered radical cations [108,136]. Compared with the parent compound, **TP777** has slightly simpler structures and are more prone to further oxidative decomposition. It should be noted that **TP777** is also

detected in the UV/ H_2O_2 reaction system [137]. Therefore, it can be speculated that the side chain of contrast compound can also be demethylated upon the oxidation of $\text{HO}^\bullet$.

Iomeprol with high water solubility is an isomer of iopamidol. The destruction pathways of iomeprol in the AOPs system are shown in route (c). Unlike iopromide and iopamidol, the hydrogen in the alcohol group of iomeprol side chain is extracted to form the corresponding ketone group (**TP775**), and this change usually occurs in the $\text{HO}^\bullet$ -mediated system. The oxidation of primary alcohol groups to carboxyl groups is an important pathway that cannot be ignored. Carboxyl by-products formed by the oxidation of primary alcohol groups were detected in both UV/ Fe^{2+} / H_2O_2 system ($\text{HO}^\bullet$ system) and Co/PMS system $\text{SO}_4^{\cdot-}$ mediate system [119,138]. This was confirmed by the detected intermediates **TP793** and **TP809**. Furthermore, by-products containing carboxyl groups formed by the oxidation of primary alcohol groups also appear in the biodegradation processes of ICMs [139]. In addition to the alcohol group, there are amide bonds in the side chain of iomeprol. The dealkylation process results in the conversion of alkyl ($-\text{CH}_2(\text{CHOH})\text{CH}_2\text{OH}$) aromatic amide to an aromatic carbamoyl. The dealkylation reaction is consistent with recent studies on ICMs degradation [139,140]. Dong *et al.* and Wendel *et al.* reported that in the iron-activated persulfate system, dealkylation occurred via chlorination during the degradation of iopamidol [118,119,140]. The electron is transferred from the amine nitrogen to N-center free radical generated by the $\text{SO}_4^{\cdot-}$, which is rapidly hydrolyzed to hydroxylamine by aniline radical intermediate, and the hydroxylamine derivative can be further oxidized to nitro derivative **TP750** through the nitroso intermediate [108,141]. Both $\text{SO}_4^{\cdot-}$ and the $\text{HO}^\bullet$ can initiate the oxidation of the amine groups attached to the benzene ring to nitro groups, as confirmed in previous studies [116,141–143].

5. Conclusion and perspectives

ICMs, as emerging environmental contaminants, are recalcitrant and can persist in the environment. Although many literatures on the contrast agents are available now, there is a lack of systematic studies on ICMs (including reveal-time detection of ICMs concentration levels and efficient removal of ICMs). Contrast media are accumulated in the environment due to the dual factors of high utilization rate and low removal rate, which results a growing contamination of ICMs. Various degradation processes have different degrees of ICMs destruction, depending on the oxidant and other reaction conditions. Since a single AOP is susceptible to environmental factors affecting ICMs degradation, the removal of ICMs by combined AOPs would be more efficient. In particular, the combination of electrooxidation and other AOPs is a promising treatment process because of its simple operation, rapid reaction, complete destruction and no waste stream. ICMs are degraded mainly through deiodination, decarboxylation, $\text{HO}^\bullet$ addition, oxidation of alcohol groups, amide bond cleavage and amino oxidation. Ionic ICMs are more difficult to remove than non-ionic ICMs. The removal rate of AOPs for ionic ICMs hardly exceeds 80%, but for non-ionic ICMs it is above 90%. Moreover, the low TOC removal indicates that the degradation of ICMs is not caused by the destruction of the entire molecule, only by the deiodination of the benzene ring and the cleavage of side chain. This is also confirmed by the identification of iodinated by-products.

In recent years, some delightful progresses have been made in the studies of ICMs, but some deficiencies remain. First, most of the experimental data were obtained in ultrapure water, which cannot represent the real situation in natural water environment. Secondly, the existing ICMs detection methods have great limitations and cannot monitor the real concentration profile of ICMs in real time, which is not conducive to a comprehensive

understanding of the pollution status of ICMs. Besides, there are no relevant data on ICMs contamination in sludge, and it is unknown whether ICMs in the aquatic environment is involved in the water cycle. Finally, the information on the degradation mechanism and degradation kinetics of ICMs is incomplete, and the toxicity assessment of the degradation products of AOPs is scarce. In summary, it is necessary to expand the research scope, optimize the ICMs detection and removal methods, make up for the gaps in the detection methods and removal processes, supplement experimental data, and provide reference information for subsequent research. Furthermore, it may be feasible to optimize ICMs molecular structures or find substitute for ICMs to reduce the contamination of ICMs from the source.

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.

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References

- [1] I. Arslan-Alaton, T. Olmez-Hanci, G. Korkmaz, C. Sahin, *Chem. Eng. J.* 318 (2017) 64–75.
- [2] W. Bottinor, P. Polkampally, I. Jovin, *Int. J. Angiol.* 22 (2013) 149–154.
- [3] T.A. Ternes, R. Hirsch, *Environ. Sci. Technol.* 34 (2000) 2741–2748.
- [4] T. Steger-Hartmann, R. Laange, H. Schweinfurth, M. Tschampel, I. Rehmann, *Water Res.* 36 (2002) 266–274.
- [5] S.B. Yu, A.D. Watson, *Chem. Rev.* 99 (1999) 2353–2377.
- [6] K.G. Estep, K.A. Josef, E.R. Bacon, et al., *J. Med. Chem.* 43 (2000) 1940–1948.
- [7] W. Zhang, I. Soutrel, A. Amrane, F. Fourcade, F. Geneste, *Front. Chem.* 8 (2020) 646.
- [8] C.Y. Hu, Y.Z. Hou, Y.L. Lin, et al., *Chemosphere* 229 (2019) 602–610.
- [9] C.Y. Hu, S.C. Ren, Y.L. Lin, et al., *J. Water Reuse Desal.* 11 (2021) 560–571.
- [10] S.E. Duijk, C. Lindell, C.C. Cornelison, et al., *Environ. Sci. Technol.* 45 (2011) 6845–6854.
- [11] T. Ye, B. Xu, Z. Wang, et al., *Water Res.* 66 (2014) 390–398.
- [12] T. Steger-Hartmann, R. Länge, H. Schweinfurth, *Environ. Res.* 42 (1999) 274–281.
- [13] S.S. Kabirhashemi, H. Eskandari, *Sens. Actuators B: Chem.* 348 (2021) 130731.
- [14] S. Gartsier, L. Brinker, T. Erbe, K. Kummerer, R. Willmund, *Acta Hydroch. Hydrob.* 24 (1996) 90–97.
- [15] K. Kuemmerer, T. Erbe, S. Gartsier, L. Brinker, *Chemosphere* 36 (1998) 2437–2445.
- [16] T.E. Doll, F.H. Frimmel, *Water Res.* 38 (2004) 955–964.
- [17] A. Putschew, S. Wischnack, M. Jekel, *Environ. Sci. Technol.* 255 (2000) 129–134.
- [18] S.D. Richardson, F. Fasano, J.J. Ellington, et al., *Environ. Sci. Technol.* 42 (2008) 8330–8338.
- [19] H. Dong, Z. Qiang, J. Lian, et al., *Water Res.* 129 (2018) 319–326.
- [20] S. Pérez, D. Barceló, *Anal. Bioanal. Chem.* 387 (2007) 1235–1246.
- [21] W. Kalsch, *Sci. Total Environ.* 225 (1999) 143–153.
- [22] T. Erbe, K. Kuemmerer, S. Gartsier, L. Brinker, *Fortschr. Röntgenstr.* 169 (1998) 420–423.
- [23] T.A. Ternes, *Water Res.* 32 (1998) 3245–3260.
- [24] D. Kanakaraju, B.D. Glass, M. Oelgemoller, *J. Environ. Manage.* 219 (2018) 189–207.
- [25] S. Perez, P. Eichhorn, M.D. Celiz, D.S. Aga, *Anal. Chem.* 78 (2006) 1866–1874.
- [26] G. Teijon, L. Candela, K. Tamoh, A. Molina-Diaz, A.R. Fernandez-Alba, *Sci. Total Environ.* 408 (2010) 3584–3595.
- [27] S. Schittko, A. Putschew, M. Jekel, *Water Sci. Technol.* 50 (2004) 261–268.
- [28] D. Weissbrodt, L. Kovalova, C. Ort, et al., *Environ. Sci. Technol.* 43 (2009) 4810–4817.
- [29] K. Nodler, T. Licha, K. Bester, M. Sauter, *J. Chromatogr. A* 1217 (2010) 6511–6521.
- [30] A. Tiehm, N. Schmidt, M. Stieber, et al., *Water Resour. Manage.* 25 (2011) 1195–1203.
- [31] I.J. Lopez-Prieto, S. Wu, W. Ji, K.D. Daniels, S.A. Snyder, *Chemosphere* 243 (2020) 125311.
- [32] A. Sengar, A. Vijayanandan, *Sci. Total Environ.* 769 (2021) 144846.
- [33] A. Sengar, A. Vijayanandan, *Sci. Total Environ.* 807 (2022) 150677.
- [34] Y. Watanabe, L.T. Bach, P. Van Dinh, et al., *Arch. Environ. Contam. Toxicol.* 70 (2016) 671–681.
- [35] B. Yao, S. Yan, L. Lian, et al., *Environ. Pollut.* 236 (2018) 889–898.
- [36] Y.Y. Yang, J.L. Zhao, Y.S. Liu, et al., *Sci. Total Environ.* 616–617 (2018) 816–823.
- [37] T. Azuma, K. Otomo, M. Kunitou, et al., *Sci. Total Environ.* 657 (2019) 476–484.
- [38] D. Fabbri, P. Calza, D. Dalmasso, et al., *Sci. Total Environ.* 572 (2016) 340–351.
- [39] K. Nodler, D. Voutsas, T. Licha, *Mar. Pollut. Bull.* 85 (2014) 50–59.
- [40] C. Valls-Cantenys, M. Scheurer, M. Iglesias, et al., *Anal. Bioanal. Chem.* 408 (2016) 6189–6200.
- [41] R. Münze, C. Hannemann, P. Orlinskiy, et al., *Sci. Total Environ.* 599 (2017) 387–399.
- [42] K. Ribbers, L. Breuer, R.A. During, *Chemosphere* 218 (2019) 189–196.
- [43] J.L. Kormos, M. Schulz, T.A. Ternes, *Environ. Sci. Technol.* 45 (2011) 8723–8732.
- [44] L. Wolf, C. Zwiener, M. Zemmann, *Sci. Total Environ.* 430 (2012) 8–19.
- [45] L. Candela, K. Tamoh, I. Vadillo, J. Valdes-Abellan, *Environ. Earth Sci.* 75 (2016) 244.
- [46] W. Seitz, R. Winzenbacher, *Environ. Monit. Assess.* 189 (2017) 244.
- [47] D. Simazaki, R. Kubota, T. Suzuki, et al., *Water Res.* 76 (2015) 187–200.
- [48] Z. Xu, X. Li, X. Hu, D. Yin, *Chemosphere* 184 (2017) 253–260.
- [49] W. Ens, F. Sennner, B. Gygas, G. Schlotterbeck, *Anal. Bioanal. Chem.* 406 (2014) 2789–2798.
- [50] A. Mendoza, B. Zonja, N. Mastroianni, et al., *Environ. Int.* 86 (2016) 107–118.
- [51] T. Azuma, K. Otomo, M. Kunitou, et al., *Sep. Purif. Technol.* 212 (2019) 483–489.
- [52] T.A. Ternes, J. Stüber, N. Herrmann, et al., *Water Res.* 37 (2003) 1976–1982.
- [53] R. Andreozzi, V. Caprio, A. Insola, R. Marotta, *Catal. Today* 53 (1999) 51–59.
- [54] B. Legube, N.K.V. Leitner, *Catal. Today* 53 (1999) 61–72.
- [55] F.J. Beltran, F.J. Rivas, R. Montero-de-Espinosa, *Appl. Catal. B: Environ.* 39 (2002) 221–231.
- [56] S.J. Masten, S.H.R. Davies, *Environ. Sci. Technol.* 28 (1994) 180–185.
- [57] U. Von Gunten, *Water Res.* 37 (2003) 1443–1467.
- [58] M.O. Buffle, J. Schumacher, S. Meylan, M. Jekel, U. von Gunten, *Ozone Sci. Eng.* 28 (2006) 247–259.
- [59] T. Matsushita, M. Hashizuka, T. Kuriyama, Y. Matsui, N. Shirasaki, *Chemosphere* 148 (2016) 233–240.
- [60] M.M. Huber, A.G. Bel, A. Joss, et al., *Environ. Sci. Technol.* 39 (2005) 4290–4299.
- [61] W. Seitz, J.Q. Jiang, W. Schulz, et al., *Chemosphere* 70 (2008) 1238–1246.
- [62] L. Kovalova, H. Siegrist, U. von Gunten, et al., *Environ. Sci. Technol.* 47 (2013) 7899–7908.
- [63] L. Ferrando-Climent, R. Gonzalez-Olmos, A. Anfruns, et al., *Chemosphere* 168 (2017) 284–292.
- [64] J.L. Acero, U. Von Gunten, *J. Am. Water Works Assoc.* 93 (2001) 90–100.
- [65] R. Gulde, B. Clerc, M. Rutsch, et al., *Water Res.* 207 (2021) 117812.
- [66] A.D. Bokare, W. Choi, *J. Hazard. Mater.* 275 (2014) 121–135.
- [67] N.N. Wang, T. Zheng, G.S. Zhang, P. Wang, *J. Environ.* 4 (2016) 762–787.
- [68] I. Velo-Gala, J.J. López-Peñalver, M. Sánchez-Polo, J. Rivera-Utrilla, *Chem. Eng. J.* 241 (2014) 504–512.
- [69] X. Tao, J.M. Su, J.F. Chen, J.C. Zhao, *Chem. Commun.* 36 (2005) 4607–4609.
- [70] F.J. Real, F.J. Benitez, J.L. Acero, J.J.P. Sagasti, F. Casas, *Ind. Eng. Chem. Res.* 48 (2009) 3380–3388.
- [71] E. Bocos, N. Oturan, M. Pazos, M.A. Sanroman, M.A. Oturan, *Environ. Sci. Pollut. Res. Int.* 23 (2016) 19134–19144.
- [72] J. Jeong, J. Yoon, *Water Res.* 39 (2005) 2893–2900.
- [73] Y. Zuo, J. Zhan, *Atmos. Environ.* 39 (2005) 27–37.
- [74] F. Gulshan, S. Yanagida, Y. Kameshima, et al., *Water Res.* 44 (2010) 2876–2884.
- [75] C. Zhao, L.E. Arroyo-Mora, A.P. DeCaprio, et al., *Water Res.* 67 (2014) 144–153.
- [76] T.E. Doll, F.H. Frimmel, *Chemosphere* 52 (2003) 1757–1769.
- [77] M. Sprehe, S.U. Geißen, A. Vogelpohl, *Water Sci. Technol.* 44 (2001) 317–323.
- [78] G. Prados-Joya, M. Sanchez-Polo, J. Rivera-Utrilla, M. Ferro-Garcia, *Water Res.* 45 (2011) 393–403.
- [79] T.E. Doll, F.H. Frimmel, *Water Res.* 39 (2005) 403–411.
- [80] M.N. Sugihara, D. Moeller, T. Paul, T.J. Strathmann, *Appl. Catal. B: Environ.* 129 (2013) 114–122.
- [81] J.M. Herrmann, *Catal. Today* 54 (1999) 115–129.
- [82] J.Z. Zhang, *J. Phys. Chem. B* 103 (2000) 7239–7253.
- [83] D.D. Dionysiou, M.T. Suidan, I. Baudin, J.M. Laine, *Appl. Catal. B: Environ.* 50 (2004) 259–269.
- [84] K.A. Hislop, J.R. Bolton, *Environ. Sci. Technol.* 33 (1999) 3119–3126.
- [85] A.K. Biñ, S. Sobera-Madej, *Ozone Sci. Eng.* 34 (2012) 136–139.
- [86] X.X. He, M. Pelaez, J.A. Westrick, et al., *Water Res.* 46 (2012) 1501–1510.
- [87] X. Zhao, J. Jiang, S. Pang, et al., *Chemosphere* 221 (2019) 270–277.
- [88] C.C. Wong, W. Chu, *Environ. Sci. Technol.* 37 (2003) 2310–2316.
- [89] S. Perez, P. Eichhorn, V. Ceballos, D. Barcelo, *J. Mass Spectrom.* 44 (2009) 1308–1317.
- [90] M. Sprehe, S.U. Geissen, A. Vogelpohl, *Water Sci. Technol.* 44 (2001) 317–323.
- [91] E. Borowska, E. Felis, S. Zabczynski, *Water Air Soil Pollut.* 226 (2015) 151.
- [92] C. Sichel, C. Garcia, K. Andre, *Water Res.* 45 (2011) 6371–6380.
- [93] X. Kong, J. Jiang, J. Ma, Y. Yang, S. Pang, *Chemosphere* 193 (2018) 655–663.
- [94] C.Y. Hu, Y.Z. Hou, Y.L. Lin, A.P. Li, Y.G. Deng, *Chemosphere* 360 (2019) 1003–1010.
- [95] G.V. Buxton, C.L. Greenstock, W.P. Helman, A.B. Ross, *J. Phys. Chem.* 17 (1988) 514–886.
- [96] S.J. Zhang, H. Jiang, M.J. Li, et al., *Environ. Sci. Technol.* 41 (2007) 1977–1982.

- [97] Q. Zhao, R. Goto, T. Saito, T. Kobayashi, T. Sasaki, *Chemosphere* 256 (2020) 127021.
- [98] Q. Zhao, T. Kobayashi, T. Saito, T. Sasaki, *J. Hazard. Mater.* 411 (2021) 125071.
- [99] J. Jeong, J. Jung, W.J. Cooper, *Water Res.* 44 (2010) 4391–4398.
- [100] I. Velo-Gala, J.J. López-Peñalver, M. Sánchez-Polo, J. Rivera-Utrilla, *Chem. Eng. J.* 195–196 (2012) 369–376.
- [101] N. Getoff, W. Lutz, *Radiat. Phys. Chem.* 25 (1985) 21–26.
- [102] S.P. Mezyk, J.R. Peller, S.K. Cole, et al., *Ozone Sci. Eng.* 30 (2008) 58–64.
- [103] G. Zhao, Y. Pang, L. Liu, J. Gao, B. Lv, *J. Hazard. Mater.* 179 (2010) 1078–1083.
- [104] C. Zwiener, T. Glauner, J. Sturm, M. Worner, F.H. Frimmel, *Anal. Bioanal. Chem.* 395 (2009) 1885–1892.
- [105] E. Brillas, C.A. Martínez-Huitle, *Appl. Catal. B: Environ.* 166–167 (2015) 603–643.
- [106] M. Moura de Salles Pupo, J.M. Albahaca Oliva, K.I. Barrios Eguiluz, G.R. Salazar-Banda, J. Radjenovic, *Chemosphere* 253 (2020) 126701.
- [107] X.D. Lv, S.Q. Yang, W.J. Xue, Y.H. Cui, Z.Q. Liu, *J. Hazard. Mater.* 366 (2019) 250–258.
- [108] J. Radjenovic, M. Petrovic, *Water Res.* 94 (2016) 128–135.
- [109] G. Del Moro, C. Pastore, C. Di Iaconi, G. Mascolo, *Sci. Total Environ.* 506–507 (2015) 631–643.
- [110] O. Turkyay, S. Barisci, E. Ulusoy, A. Dimoglo, *Water Air Soil Pollut.* 229 (2018) 170–181.
- [111] M. Zaghdoudi, F. Fourcade, I. Soutrel, et al., *J. Hazard. Mater.* 335 (2017) 10–17.
- [112] F. Geneste, *Curr. Opin. Electrochem.* 11 (2018) 19–24.
- [113] C. Lutke Eversloh, N. Henning, M. Schulz, T.A. Ternes, *Water Res.* 48 (2014) 237–246.
- [114] E. Hapeshi, A. Lambrianides, P. Koutsoftas, et al., *Environ. Sci. Pollut. Res. Int.* 20 (2013) 3592–3606.
- [115] G.P. Anipsitakis, D.D. Dionysiou, *Appl. Catal. B: Environ.* 54 (2004) 155–163.
- [116] M.M. Ahmed, S. Barbati, P. Doumenq, S. Chiron, *Chem. Eng. J.* 197 (2012) 440–447.
- [117] Y. Gao, Z. Zhang, S. Li, et al., *Appl. Catal. B: Environ.* 185 (2016) 22–30.
- [118] H.Y. Dong, Z.M. Qiang, J. Hu, C. Sans, *Chem. Eng. J.* 316 (2017) 288–295.
- [119] X.X. Wang, Z.H. Wang, Y.Z. Tang, et al., *Chem. Eng. J.* 368 (2019) 999–1012.
- [120] M.V. Alipázaga, N. Coichev, *Anal. Lett.* 36 (2003) 2255–2275.
- [121] X. Zhao, W. Wu, Y. Yan, *Environ. Sci. Pollut. Res.* 26 (2019) 24707–24719.
- [122] D. Zhou, Y. Yuan, S. Yang, H. Gao, L. Chen, *J. Sulfur Chem.* 36 (2015) 373–384.
- [123] J.P. Zhu, Y.L. Lin, T.Y. Zhang, et al., *Chem. Eng. J.* 367 (2019) 86–93.
- [124] W.T. Shang, Z.J. Dong, M. Li, et al., *Chem. Eng. J.* 361 (2019) 1333–1344.
- [125] Y. Gao, W. Fan, Z. Zhang, et al., *J. Hazard. Mater.* 426 (2022) 128114.
- [126] T.W. Chan, N.J. Graham, W. Chu, *J. Hazard. Mater.* 181 (2010) 508–513.
- [127] J.A. Khan, X.X. He, N.S. Shah, et al., *Chem. Eng. J.* 252 (2014) 393–403.
- [128] L. Zhou, C. Ferronato, J.M. Chovelon, M. Sleiman, C. Richard, *Chem. Eng. J.* 311 (2017) 28–36.
- [129] Y. Guo, X. Lou, C. Fang, et al., *Environ. Sci. Technol.* 47 (2013) 11174–11181.
- [130] Y. Yang, J. Jiang, X. Lu, J. Ma, Y. Liu, *Environ. Sci. Technol.* 49 (2015) 7330–7339.
- [131] Y. Mao, H. Dong, S. Liu, L. Zhang, Z. Qiang, *Water Res.* 173 (2020) 115615.
- [132] C. Liang, Z.S. Wang, C.J. Bruell, *Chemosphere* 66 (2007) 106–113.
- [133] G.D. Fang, D.D. Dionysiou, D.M. Zhou, et al., *Chemosphere* 90 (2013) 1573–1580.
- [134] F.X. Tian, B. Xu, Y.L. Lin, et al., *Water Res.* 58 (2014) 198–208.
- [135] L. Meng, S. Yang, C. Sun, et al., *J. Hazard. Mater.* 337 (2017) 34–46.
- [136] R. Chahboune, H. Mountacer, M. Sarakha, *Rapid Commun. Mass Spectrom.* 29 (2015) 1370–1380.
- [137] R.R. Singh, Y. Lester, K.G. Linden, et al., *Environ. Sci. Technol.* 49 (2015) 2983–2990.
- [138] S. Giannakis, M. Jovic, N. Gasilova, et al., *J. Environ. Manage.* 195 (2017) 174–185.
- [139] J.L. Kormos, M. Schulz, H.P. Kohler, T.A. Ternes, *Environ. Sci. Technol.* 44 (2010) 4998–5007.
- [140] F.M. Wendel, C. Lutke Eversloh, E.J. Machek, et al., *Environ. Sci. Technol.* 48 (2014) 12689–12697.
- [141] A.R. Becker, L.A. Sternson, *Proc. Natl. Acad. Sci. U. S. A.* 78 (1981) 2003–2007.
- [142] X.L. Zou, T. Zhou, J. Mao, X.H. Wu, *Chem. Eng. J.* 257 (2014) 36–44.
- [143] W.S. Chen, C.P. Huang, *Chem. Eng. J.* 266 (2015) 279–288.