



Oxidation processes and me

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ABSTRACT

This publication summarizes my journey in the field of chemical oxidation processes for water treatment over the last 30+ years. Initially, the efficiency of the application of chemical oxidants for micropollutant abatement was assessed by the abatement of the target compounds only. This is controlled by reaction kinetics and therefore, second-order rate constant for these reactions are the pre-requisite to assess the efficiency and feasibility of such processes. Due to the tremendous efforts in this area, we currently have a good experimental data base for second-order rate constants for many chemical oxidants, including radicals. Based on this, predictions can be made for compounds without experimental data with Quantitative Structure Activity Relationships with Hammett/Taft constants or energies of highest occupied molecular orbitals from quantum chemical computations. Chemical oxidation in water treatment has to be economically feasible and therefore, the extent of transformation of micropollutants is often limited and mineralization of target compounds cannot be achieved under realistic conditions. The formation of transformation products from the reactions of the target compounds with chemical oxidants is inherent to oxidation processes and the following questions have evolved over the years: Are the formed transformation products biologically less active than the target compounds? Is there a new toxicity associated with transformation products? Are transformation products more biodegradable than the corresponding target compounds? In addition to the positive effects on water quality related to abatement of micropollutants, chemical oxidants react mainly with water matrix components such as the dissolved organic matter (DOM), bromide and iodide. As a matter of fact, the fraction of oxidants consumed by the DOM is typically > 99%, which makes such processes inherently inefficient. The consequences are loss of oxidation capacity and the formation of organic and inorganic disinfection byproducts also involving bromide and iodide, which can be oxidized to reactive bromine and iodine with their ensuing reactions with DOM. Overall, it has turned out in the last three decades, that chemical oxidation processes are complex to understand and to manage. However, the tremendous research efforts have led to a good understanding of the underlying processes and allow a widespread and optimized application of such processes in water treatment practice such as drinking water, municipal and industrial wastewater and water reuse systems.

1. Introduction

The introduction of chemical oxidants such as chlorine, chlorine dioxide and ozone in water treatment systems in the early 20. century was triggered by the need to mitigate waterborne diseases and was a huge step forward in the provision of safe drinking water (McGuire, 2006). Chemical oxidants also have other favorable properties and were later applied for the oxidation of aesthetically/toxicologically undesired inorganic compounds such as iron(II), manganese(II), nitrite, sulfide, sulfur-based taste and odor compounds and color (Fig. 1) (Allard et al., 2013; Bruchet and Duguet, 2004; Deborde and von Gunten, 2008; Hoigné et al., 1985; Peter and von Gunten, 2007; Sain and Dietrich,

2015; Yu et al., 2015). At around the 1980s, as a consequence of the discovery of synthetic organic micropollutants by modern analytical tools, chemical oxidation processes were applied for the abatement of such compounds in drinking water (Richardson and Ternes, 2022; Schwarzenbach et al., 2006) (Fig. 1). Chemical disinfection of wastewaters has been a common practice since the beginning of the 20th century (Janex et al., 2000; Leong et al., 2008; Sawyer, 1957; Xu et al., 2002) and since the late 1990s oxidation processes are also implemented for advanced wastewater treatment to abate micropollutants (Eggen et al., 2014; Huber et al., 2003, 2005; Joss et al., 2008; Ternes et al., 2004) (Fig. 1).

To achieve the best results for water quality, a tremendous research

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effort was carried out with the goal to find the perfect chemical oxidant, which can abate micropollutants to harmless transformation products and at the same time has limited formation of disinfection byproducts from water matrix components (von Gunten, 2018). In the following, transformation products (TPs) are defined as being formed from chemical oxidation of micropollutants and disinfection byproducts (DBPs) from the oxidation of matrix components.

For the assessment of the abatement of micropollutants, the following aspects need to be considered by a multidisciplinary approach (Fig. 2) (Lee et al., 2023; Lee and von Gunten, 2016; von Gunten, 2018): (i) Kinetics of the transformation reactions of target compounds which is crucial for the efficiency, (ii) kinetics and mechanisms of TPs formation, (iii) assessment of biological effects/toxicology of TPs, and (iv) degradability of TPs in biological post-treatment. The investigation of these aspects requires laboratory experiments including many different tools such as equipment for determination of rate constants (including quench-flow and/or stopped-flow, laser flash photolysis and pulse radiolysis), prediction of rate constants by quantitative structure activity relationships (QSAR) and quantum chemical computations, advanced analytical tools to determine transformation products (e.g., LC-HRMS/MS, GC-MS, NMR), bioassays and theoretical (including *in silico*) considerations (Fig. 2) (Dodd et al., 2006, 2009; Gulde et al., 2021a, 2021b; Hübner et al., 2015; Lange et al., 2006; Lee et al., 2008; Lee and von Gunten, 2012; Mestankova et al., 2011, 2016, 2014; Mestankova et al., 2012; Minakata and Crittenden, 2011; Minakata et al., 2014; Minakata and von Gunten, 2023).

In addition to the reactions of chemical oxidants with micropollutants, they react with water matrix components such as dissolved organic matter (DOM), bromide, iodide and nitrite leading to (i) a limited stability and exposure of oxidants and (ii) the formation of DBPs from the reactions of chemical oxidants with matrix components (Abdighahroudi et al., 2021; Houska et al., 2023; Krasner, 2009; Li and Mitch, 2018; Manasfi et al., 2023; Richardson and Ternes, 2022; Sedlak and von Gunten, 2011; von Gunten, 2003, 2018).

2. Personal perspective

When I started to work in the field of oxidation processes in the early 1990s, the abatement of micropollutants by chemical oxidation was considered as the solution to the problem of organic contaminants. During my career, I had the opportunity to be part of this field and help shape the discovery of the different aspects outlined in Fig. 2 related to reactions of chemical oxidants with micropollutants and matrix components and in this publication, I will provide some of the highlights of this journey.

3. Abatement of micropollutants – kinetics

In the 1990s, the world of oxidative water treatment was much different from today. There was only limited information available on transformation product formation from oxidative degradation of target micropollutants and their abatement was considered as the solution to the contaminant problem (Duguet et al., 1990; Glaze, 1986; Hoigné and Bader, 1983a; 1983b; Peyton et al., 1982). Therefore, initially the main focus was on the determination of second-order rate constants for the abatement of micropollutants by various oxidants. Today, there is a good knowledge base with several thousand second-order rate constants in data bases, books and review papers (Table 1) (Buxton et al., 1988; Deborde and von Gunten, 2008; Hoigné and Bader, 1983a; 1983b; 1994; Hoigné et al., 1985; Lee et al., 2020a; NIST, 1995; Sharma et al., 2015; von Sonntag and von Gunten, 2012; Waldemer and Tratnyek, 2006).

From the reported second-order rate constants in literature it can be concluded that there are big differences in selectivity of the studied chemical oxidants, which will determine their applicability for the abatement of a broad range of micropollutants (Minakata and von Gunten, 2023). Generally, conventional oxidants such as ozone, chlorine and chlorine dioxide are quite selective with higher reactivities with electron-rich moieties such as activated aromatic functional groups, olefins, neutral amines and reduced sulfur species, whereas all other moieties have only limited reactivities. For a broad applicability, chemical oxidants with a wide range of reactivities are preferred and the applicability of conventional and novel oxidants decreases in the order ozone > chlorine dioxide > ferrate(VI) > permanganate > chlorine (Minakata and von Gunten, 2023). Ozone has an additional feature by formation of hydroxyl radicals ($\bullet\text{OH}$) during its decomposition in water, combining direct ozone-induced oxidation of certain functional groups (with higher efficiency) with the strong but less selective oxidation by $\bullet\text{OH}$ (Bourgin et al., 2017; Elovitz and von Gunten, 1999; Hoigné and Bader, 1975; von Sonntag and von Gunten, 2012). Processes with in situ formation of $\bullet\text{OH}$ are generally called advanced oxidation processes (AOPs) and they have been introduced in the 1980s as a solution for micropollutants which are recalcitrant to conventional oxidants (Glaze et al., 1987; Stefan, 2018). Initially, process combinations with hydrogen peroxide (H_2O_2) such as $\text{O}_3/\text{H}_2\text{O}_2$ and $\text{UV}/\text{H}_2\text{O}_2$ were introduced and more recently chlorine-based processes ($\text{UV}/\text{chlorine}$) were added to this portfolio (De Laat and Stefan, 2018; Young et al., 2018; Zhang et al., 2016). For $\text{O}_3/\text{H}_2\text{O}_2$ or $\text{UV}/\text{H}_2\text{O}_2$, O_3 and $\bullet\text{OH}$ or UV and $\bullet\text{OH}$, respectively lead to an enhancement of micropollutant abatement (Lee et al., 2017b; von Sonntag, 2008), whereas in $\text{UV}/\text{chlorine}$, $\bullet\text{OH}$, chlorine/bromine-based radicals and ozone are formed (Bulman et al., 2019; Lee et al., 2020b; Remucal and Manley, 2016). Furthermore,

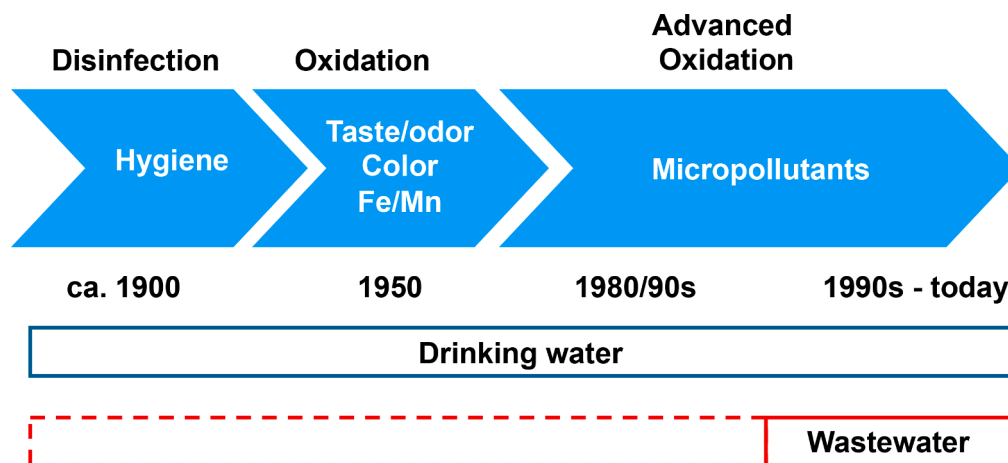


Fig. 1. Evolution of the application of chemical oxidants in municipal water and wastewater treatment from the beginning of the 20th century to today. In wastewater, disinfection was also applied from the beginning of the 20th century, however oxidation of MPs only started in the late 1990s.

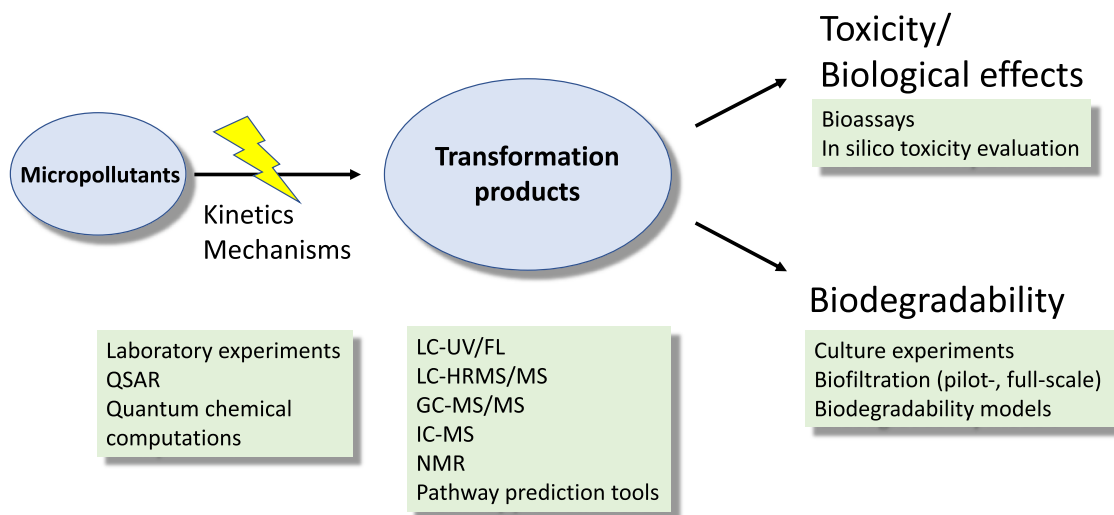


Fig. 2. Assessment of the abatement of micropollutants during chemical oxidation processes: A multidisciplinary endeavor. LC: Liquid chromatography; UV: Detection by absorption in the UV range; FL: fluorescence detection; MS: mass spectrometry; HRMS: high resolution MS; GC: gas chromatography; IC: ion chromatography; NMR: nuclear magnetic resonance.

Table 1

Estimated number of available second-order rate constants for the reactions of different chemical oxidants with inorganic and organic compounds from the cited literature in the text.

Chemical oxidant	Number of available second-order rate constants k
Hydroxyl radical	~ 2000
Ozone	~ 500
Chlorine	~ 300
Chlorine dioxide	~ 100
Permanganate	~ 50
Ferrate(VI)	~ 50
Sulfate radical	~ 50

processes based on sulfate radicals have shown promise for water treatment, however, are not widely applied in full-scale treatment yet (Lee et al., 2020a). Finally, other processes based on catalytic/heterogeneous ozonation, and activation of ferrate(VI) and permanganate have been investigated, however, their applicability to real water treatment systems needs further investigations (Guo et al., 2021; Li et al., 2015; Nie et al., 2014; Song et al., 2015; Wang et al., 2022; Xu and von Gunten, 2021).

Second-order rate constants k for the reactions of chemical oxidants with micropollutants span over a wide range from very low ($< 0.1 \text{ M}^{-1}\text{s}^{-1}$) to diffusion-controlled reactions with $k \sim 10^{10} \text{ M}^{-1}\text{s}^{-1}$. The abatement of micropollutants by chemical oxidants typically follows second-order kinetics (Eqs. (1) and (2)).

$$\frac{d[\text{MP}]}{dt} = -k[\text{MP}][\text{ox}] \quad (1)$$

$$\ln\left(\frac{[\text{MP}]}{[\text{MP}]_0}\right) = -k[\text{ox}]t \quad (2)$$

Where MP = micropollutant, ox = chemical oxidant, k = second-order rate constant for the reaction of an oxidant with MP, t = reaction time.

To assess the efficiency of oxidative MP abatement, the half-life time ($t_{1/2}$) can be calculated, which corresponds to the time required to degrade a compound to half of its original concentration (eq. (3)).

$$t_{1/2} = -\frac{\ln\left(\frac{1}{2}\right)}{k[\text{ox}]} = \frac{0.69}{k[\text{ox}]} \quad (3)$$

Eq. (3) shows clearly that $t_{1/2}$ depends on both k and the concentration of the oxidant, which depends strongly on the water matrix composition with typical ranges shown in Fig. 3 for conventional oxidants and radicals. Therefore, a high k value alone for the reaction of an oxidant with a micropollutant does not guarantee an efficient abatement.

It can be concluded, that radical-type reactions are only competitive compared to conventional oxidants, for high second-order rate constants. If we assume a radical concentration of 10^{-12} M and k in the range of $10^9 - 10^{10} \text{ M}^{-1}\text{s}^{-1}$ (grey box, Fig. 3) the half-life time is similar

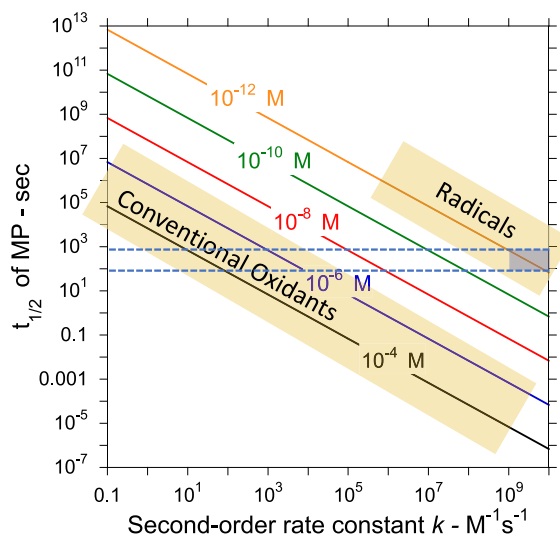


Fig. 3. Half-life time (sec) of a micropollutant (MP) as a function of the oxidant concentrations ($10^{-4} - 10^{-12} \text{ M}$, depends strongly on the water matrix composition) and the second-order rate constants k ($10^{-1} - 10^{10} \text{ M}^{-1}\text{s}^{-1}$). The range of concentrations and k for conventional oxidants and radicals is shown in the yellow boxes. The grey box shows a typical range of radical concentrations. The intersections of the horizontal lines with the range of concentrations for conventional oxidants with the corresponding second-order rate constants show the conditions for conventional oxidants with similar $t_{1/2}$ values.

to conventional oxidants with $k = 10^2 \text{ M}^{-1}\text{s}^{-1}$ or $10^3 \text{ M}^{-1}\text{s}^{-1}$ for concentrations of 10^{-4} or 10^{-6} M , respectively (Fig. 3). This shows clearly, that radical reactions are only meaningful if conventional oxidants have limited reactivities with organic contaminants with $k < \sim 10^3 \text{ M}^{-1}\text{s}^{-1}$. Because during ozonation direct oxidation by ozone and by $\bullet\text{OH}$ occurs, this is a very efficient broadband solution for many organic contaminants (von Sonntag and von Gunten, 2012).

4. Abatement of micropollutants – mechanisms

Mineralization of micropollutants is typically not achievable during oxidative water treatment, because of the limited oxidant doses, which are restricted by economics and the formation of DBPs from reactions with matrix components (von Gunten, 2018). Therefore, during oxidation, typically TPs are formed with only partially modified structures compared to the target compounds (Acero et al., 2005, 2000; Huber et al., 2004; Lange et al., 2006; Sein et al., 2008; Stefan and Bolton, 1998; Stefan et al., 2000; von Sonntag and von Gunten, 2012). One case in point is the transformation of atrazine during ozone-based processes with the formation of transformation products with intact triazine ring structures, which still are biologically active (Acero et al., 2000; Tauber and von Sonntag, 2000). In the European Union (EU) drinking water regulation of 1998, active metabolites of pesticides were also regulated (EU, 2021) and this was a drawback for oxidative water treatment of atrazine, but potentially also for other pesticides, because of the only limited transformation of the target compounds. As a consequence, advanced oxidation processes for atrazine abatement were banned in France and this was an important trigger point from where on transformation products from oxidation of other micropollutants were considered as well (FR, 2000). Based on enhanced analytical equipment, transformation product studies became more feasible in the last decades and they led to a better understanding of oxidation reaction mechanisms (Minakata and von Gunten, 2023; von Gunten, 2018; von Sonntag and von Gunten, 2012). The most important oxidation mechanisms are

summarized in Fig. 4 for ozone, chlorine and chlorine dioxide and some radicals. The basic reactions include addition with ensuing reactions such as bond breakage or oxygen/halogen atom transfer, H-abstraction, and electron transfer (Minakata and von Gunten, 2023). For the more selective oxidants (ozone, chlorine, chlorine dioxide), typically one or a few moieties in a target compound show reactivity, but for radicals with a much lower selectivity, many different moieties may react, possibly leading to a “combinatorial explosion” of transformation products (Minakata and von Gunten, 2023). In a study on ozonation, 227 TPs could be proposed from 39 target compounds based on liquid chromatography coupled with high resolution mass spectrometry combined with knowledge of ozone and $\bullet\text{OH}$ reactions (Gulde et al., 2021a). This shows that on average about 6 transformation products per target compound were detected, but due to limitations of the analytical window, many more may not have been detected (Gulde et al., 2021a). In another study, 497 TPs were predicted from the abatement of trichloroethylene by the UV/chlorine process including reactions with $\bullet\text{OH}$, Cl^\bullet , $\text{Cl}_2^{\bullet-}$ and ClO^\bullet (Zhang et al., 2021). To further improve experimental product studies, careful investigations with close to 100% mass balances are needed. A combination of different analytical tools (LC-MS, GC-MS, IC-MS, NMR) is often necessary to achieve this goal. Furthermore, continuous improvement of the sensitivity of analytical tools in combination with advanced tools for data interpretation will lead to a detection and quantification of so far unknown transformation products.

In addition to experimental determination of transformation products, significant efforts have been made to develop prediction tools. They are based on known pathways which are combined in computer-based system for *in silico* prediction of reaction kinetics and transformation products (Guo et al., 2014; Lee et al., 2017a, 2015; Zhang et al., 2021). In combination with experimental studies, this is an interesting option for product identification. In addition, quantum chemical calculations can be applied to validate reaction mechanisms including transient products, and predict transformation pathways (Kamath et al., 2018; Minakata et al., 2017; Minakata and von Gunten,

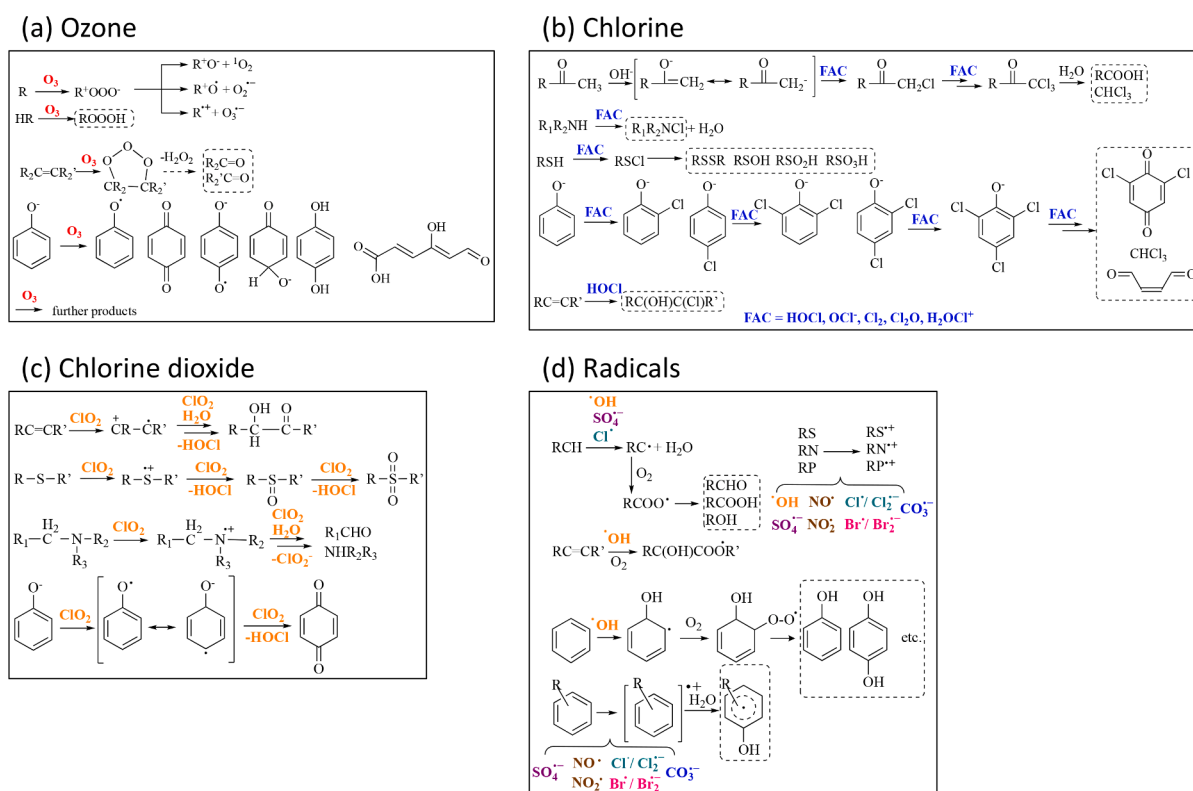


Fig. 4. Reaction mechanisms for the transformation of various organic moieties by ozone, chlorine, chlorine dioxide and the radicals $\bullet\text{OH}$, $\text{SO}_4^{\bullet-}$, Cl^\bullet , $\text{Cl}_2^{\bullet-}$, Br^\bullet , $\text{Br}_2^{\bullet-}$, $\text{NO}_2^{\bullet-}$, NO^\bullet , $\text{CO}_3^{\bullet-}$. Adapted from (Minakata and von Gunten, 2023). Copyright 2023 American Chemical Society.

2023; Tentscher et al., 2019; Trogolo et al., 2015). Furthermore, new generation models show promise. They are based on chemical reaction networks which describe chemical reaction systems by connections between reactants and products with quantum chemical approaches (Türtscher and Reiher, 2023). A combination of experimental and theoretical approaches has been shown to be most useful for kinetic and mechanistic studies of oxidation reactions.

5. Abatement of micropollutants – toxicity

The main driver for the abatement of micropollutants in aquatic systems is the reduction of the effects of biologically active compounds (von Gunten, 2018). Since many micropollutants are only partially degraded, with sometimes intact structures, the question arises if the primary biological effects are abated and/or if new effects emerge. One case in point are endocrine disruptors, which have been shown to be discharged from municipal wastewater treatment plants to aquatic ecosystems and lead to feminization in fishes at very low concentrations in the ng/L range (Jobling et al., 2003; Kidd et al., 2007). For example, it has been shown that oxidative treatment generally leads to sufficient modifications of the structures of an estrogenic compound, 17 α -ethinylestradiol, to abate the estrogenic activity completely after the first attack on this substance (Fig. 5) (Huber et al., 2004; Lee et al., 2008).

With this fortunate case in mind, further bioactive micropollutant classes, such as antimicrobial and antiviral compounds and pesticides were tested during ozonation and advanced oxidation. Also in these cases, abatement of the parent compounds was correlated with a loss of the biological activity, even though the effects sometimes only disappeared after a more extended transformation (Dodd et al., 2009, 2010; Lange et al., 2006; Mestankova et al., 2011, 2016, 2012; Suarez et al., 2007). In general, such conditions are fulfilled during oxidative water treatment. Biologically active compounds typically have very specific interactions with receptors, which are very susceptible to small changes in the molecular structures. It is unlikely, that another compound with a specific biological effect is formed by oxidative transformation. However, transformation products such as mutagens with less specific effects can be formed.

One example is the formation *N*-nitrosodimethylamine (NDMA)

during ozonation of *N,N*-dimethylsulfamide (DMS), a metabolite of the fungicide tolylfluanide, in bromide-containing waters (Fig. 6a) (Schmidt and Brauch, 2008). DMS reacts only slowly with ozone, but the bromine-activated DMS has a higher reactivity leading to the formation of NDMA with a yield of about 50%, and nitrate with an almost complete nitrogen mass balance (Trogolo et al., 2015; von Gunten et al., 2010). In this reaction, bromide acts as a catalyst and is recycled in the reaction and therefore even traces can enhance NDMA formation (Fig. 6a). Overall, when designing the fungicide tolylfluanide, a reaction sequence leading to such a problematic cocktail could not be anticipated (Fig. 6b): (i) Biological transformation of tolylfluanide to DMS, (ii) reaction of DMS with HOBr, which is formed from the O₃-Br⁻ reaction and (iii) the reaction of Br-DMS with ozone with the formation of NDMA, nitrate and release of bromide (Schmidt and Brauch, 2008; von Gunten et al., 2010). Therefore, for future accreditation of active compounds, a test with oxidative water treatment should be considered with both the primary compound and its metabolites. Such an approach has been proposed in a guidance document of the European Chemicals Agency (ECHA) and European Food Safety Authority (EFSA) in 2023 (Hofman-Caris et al., 2023).

6. Formation of transformation products – biodegradability

Ever since oxidation processes were applied for micropollutant abatement, it was considered important to combine them with a biological treatment step (Scott and Ollis, 1995). On the one hand, this is important for the biological abatement of oxygen-containing byproducts (carbonyls, carboxylic acids) from oxidation of dissolved organic matter (see below for discussion) (Hammes et al., 2006; Manasfi et al., 2023; Van der Kooij et al., 1989). On the other hand, it was claimed for decades, that oxidative TPs of micropollutants are expected to be biodegradable. Therefore, a partial oxidation of such compounds should be sufficient to remove them in biological post-treatment (Scott and Ollis, 1995). Unfortunately, this perception was partially based on a myth with limited scientific evidence. One way to assess this, is by theoretical consideration about biodegradability of organic compounds (Hübner et al., 2015). Tools to do this are mostly based on metabolic transformation of organic compounds and are not fully suited for mostly

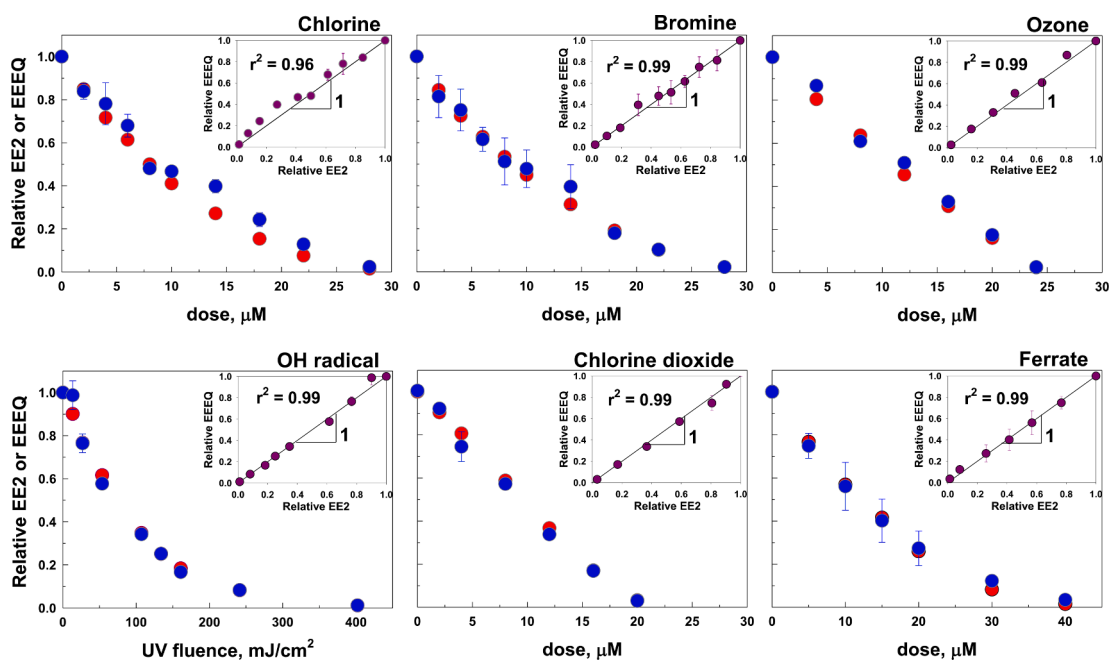


Fig. 5. Relative abatement of 17 α -ethinylestradiol (EE2, red circles) and the estrogenicity (EEEQ, Yeast Estrogen Screen (YES) Assay, blue circles) as a function of the oxidant dose in ultra-purified water at pH 8 (5 mM phosphate buffer) for chlorine, bromine, ozone, hydroxyl radical, chlorine dioxide and ferrate(VI). The insets show the correlations between the relative abatements of EE2 and EEEQ. Adapted with permission from (Lee et al., 2008). Copyright 2008 American Chemical Society.

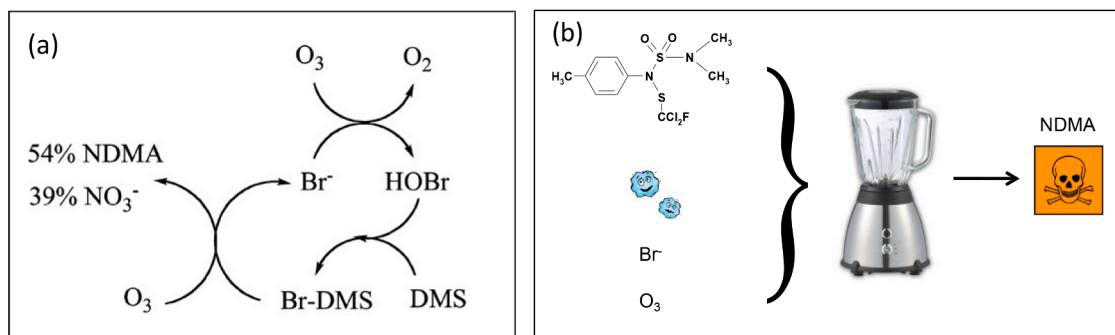


Fig. 6. NDMA and nitrate formation during ozonation of *N,N*-dimethylsulfamide (DMS)- and bromide-containing water. (a) Bromide is oxidized by ozone to HOBr, which reacts with DMS to *N*-Br-DMS. *N*-Br-DMS reacts quickly with ozone to NDMA and nitrate and releases bromide. (b) A problematic cocktail leading to a toxic compound: Microbial transformation of the fungicide tolylfluamide to DMS and the ensuing formation of *N*-Br-DMS in presence of bromide and ozone leading to NDMA as the final product.

co-metabolic transformation of low levels of TPs in municipal water/wastewater treatment (Hübner et al., 2015). Nevertheless, a theoretical assessment of TPs formed during ozonation led to the conclusion that carbonyls and carboxylic acids formed from aromatic ring opening and bond scission of olefins generally should lead to biodegradable products (Hübner et al., 2015). In contrast, ozone transformation products from compounds with amine functional groups were predicted generally not to be biodegradable. To test this experimentally, laboratory ozonation experiments were performed in synthetic waters with 51 micro-pollutants with various functional groups under mimicked realistic conditions to propose tentative transformation products based on exact masses, MS^2 fragmentation and kinetic and mechanistic considerations. 227 transformation products were tentatively identified from 39 target compounds (Gulde et al., 2021a, 2021b). There were no TPs detected from the remaining 12 target compounds, probably due to analytical shortcomings. The same experiment was repeated on a pilot plant (~ 4

m^3/h) fed with a lake water with an ozonation followed by a biological sand filtration to investigate the fate of the transformation products in an acclimatized biofilter (Gulde et al., 2021a). Only 187 of the 227 transformation products could be detected at concentrations $>$ LOD before the biofilter and therefore only they were assessed. Fig. 7 shows the relative biodegradability of the detected ozonation TPs in comparison to the parent compounds (similar, worse and better biodegradation than parent compounds). It is evident, that ozone TPs from 1°, 2°- and 3°- amine-containing moieties are generally less degradable than their parents and those of olefinic or activated aromatic moieties have a large fraction that is better biodegradable than their parents (larger green bars).

This can be explained by the formation of carbonyl-/carboxyl-type compounds during ozonation of olefins and aromatic compounds (ring opening) which are expected to be better biodegradable (Hübner et al., 2015; von Sonntag and von Gunten, 2012).

For compounds primarily reacting with hydroxyl radical (no ozone reactivity, bar on the far right, Fig. 7), which is always formed during ozonation, no general improvement of biodegradability compared to their parent compounds was observed. This means that in radical-based advanced oxidation processes the biodegradability of TPs is not expected to be better than for ozonation. From the data shown in Fig. 7 it can be concluded, that only 19% of the TPs were biodegradable and only 13% were better biodegradable than their parent compounds (Gulde et al., 2021a). Furthermore, the experimental results for biodegradation of TPs are generally in agreement with theoretical predictions, with TPs from ozonation of activated aromatic compounds and olefins having a significant and TPs from amines having a limited biodegradability. Even though there were some analytical restrictions in this study (Gulde et al., 2021a), there is a clear indication, that it cannot be generally assumed that TPs are degradable in biological post-treatment.

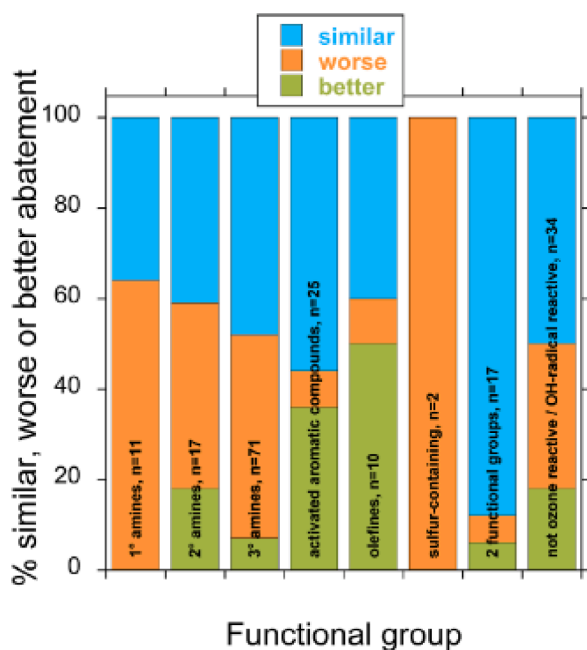


Fig. 7. Biodegradability of ozonation transformation products in a pilot-scale biofilter. 187 ozonation transformation products from 34 spiked compounds, containing various functional groups (1°, 2°, 3°-amines, activated aromatic compounds, olefins, sulfur-containing, no electron-rich functional groups) were detected and their biodegradability is shown relative to the parent compounds. From (Gulde et al., 2021a), where the experimental details are provided.

7. Formation of disinfection byproducts

7.1. Organic compounds

DOM is by far the main consumer of chemical oxidants in water and phenolic moieties which are present in $\sim 1\text{--}4$ mmol/gDOC are the most important reaction partners (Houska et al., 2021; Önnby et al., 2018). Phenolic moieties in DOM have been determined by oxidative titrations with chlorine dioxide and by the electron donating capacity (EDC) (Aeschbacher et al., 2012; Houska et al., 2021; Walpen et al., 2020). Fig. 8 shows a correlation between the phenolic content determined by chlorine dioxide titration and the EDC for various natural organic matter isolates and DOMs of real wastewaters.

If we assume a DOC concentration of 5–10 mg/L for a wastewater effluent, this results in about 20 μM of phenols, which can consume most

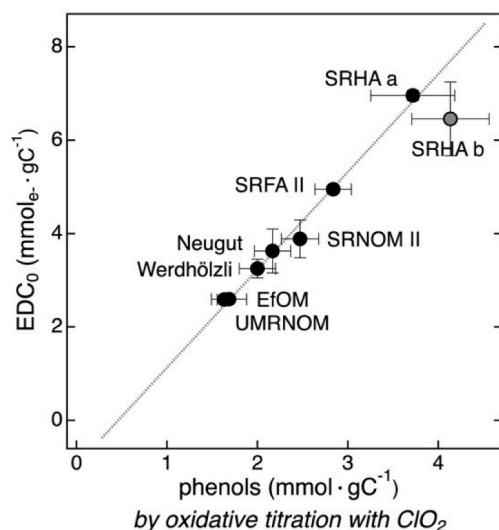


Fig. 8. Phenolic content of dissolved organic matter. Correlation between the EDC (electron donating capacity) and the phenol content determined by titration with chlorine dioxide. SRHA, SRFA, SRNOM and UMRNOM are all standards from the International Humic Substances Society, EfOM is an effluent organic matter isolate and Neugut and Werdhölzli are secondary effluents from municipal wastewater treatment plants. From (Houska et al., 2021).

chemical oxidants quite fast (Criquet et al., 2015; Deborde and von Gunten, 2008; Du et al., 2012; Hoigné and Bader, 1983b; 1994; Rebenne et al., 1996). In secondary municipal wastewater effluents, the sum of ozone-reactive micropollutants is on the order of 20 µg/L (Bourgin et al., 2018), which results in about 0.1 µM if we assume an average molecular weight of 200 g/mol. The micropollutants have diverse structures, but in a best-case scenario, we can assume that they have a reactivity similar to phenol. For ozonation as an example, the fraction of the dosed ozone reacting with micropollutants is on the order of ~ 0.5%. For radicals, such as $\cdot\text{OH}$, which also have high reactivity with other DOM moieties, the fraction reacting with micropollutants is ~ 0.2% ($k_{\text{OH,DOC}} = 2.4 \times 10^4$ (L/mg/s) (von Sonntag and von Gunten, 2012), average $k_{\text{OH,micropol}} = 5 \times 10^9$ M⁻¹s⁻¹). These numbers show that by far the highest fraction of the dosed oxidant is consumed by DOM moieties, which makes oxidation processes inherently inefficient. In addition, the switch from a selective (e.g., chlorine dioxide, ozone) to rather non-selective oxidants even deteriorates the efficiency (see also Fig. 3).

Chemical oxidants react with dissolved organic matter (DOM) by analogous reactions as with micropollutants leading to oxygen-rich and/or halogenated compounds (see Figs. 4 and 9 (NOM_{ox}, Cl-, Br-, I-org.)

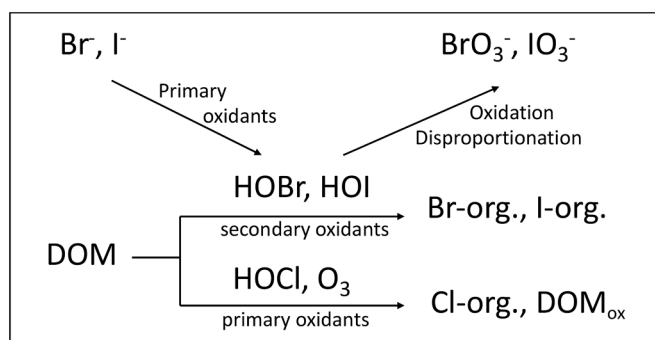


Fig. 9. Reactions of primary oxidants (e.g., HOCl, O₃) with DOM, bromide and iodide to form bromine and iodine and the ensuing chlorinated, brominated and iodinated organic compounds (Cl-, Br-, I-org.) and oxygen-rich compounds (DOM_{ox}). The formation of the inorganic DBPs bromate and iodate by oxidation and disproportionation is also shown.

with a large range of molecular weights. During chlorination and chloramination of drinking water, it has been demonstrated that the fraction < 1 kD is responsible for most of the observed toxicity (Dong et al., 2023). In a study with chlorination of iodinated X-ray contrast media lower molecular weight TPs seem toxicologically more relevant than higher molecular weight TPs (Wendel et al., 2016). In a review it was concluded that compounds with molecular weights > C₁ – C₂ are probably the main toxicity drivers of chlorine-derived DBPs (Mitch et al., 2023). Overall, combining the conclusions from these studies, it can be hypothesized that the main toxicity-driving DBPs are compounds with molecular weights in the range of 100 to a few 100 D.

One important class of compounds, which is formed by all oxidants comprises of oxygen-rich carbonyl- or carboxyl-type compounds (DOM_{ox}, Fig. 9) (Marron et al., 2020; Nawrocki et al., 2003; Richardson et al., 1999a; Swietlik et al., 2004, 2009; Wert et al., 2007). They are formed by various mechanisms from aromatic and aliphatic moieties in DOM. One case in point is the formation of carbonyl compounds during ozonation of natural waters and wastewaters. In a recent study, eight target carbonyl compounds were detected in 5 treated lake waters and wastewaters (total concentration of 280 µg/L at 1 mgO₃/mgDOC in one wastewater), and overall 178 carbonyl-type compounds were detected by a non-target analysis with derivatization with *p*-toluenesulfonylhydrazine (TSH) (Houska et al., 2023; Manasfi et al., 2023). The concentrations of these compounds are much higher than those of micropollutants and they may be responsible for the sometimes observed increase in toxicity after ozonation of e.g., wastewater (Prasse et al., 2015). Biological post-treatment generally abates toxicity (Magdeburg et al., 2014; Stalter et al., 2010a, 2011, 2010b) and it was observed that also target and non-target carbonyl compounds are efficiently abated (Manasfi et al., 2023), which is a strong indication that this class of compounds may be (partly) responsible for the observed increase in toxicity. Therefore, biological post-treatment is an efficient measure for abatement of ozonation-induced toxicity during enhanced wastewater treatment and has become a standard requirement for such processes in Switzerland (Eggen et al., 2014; Hollender et al., 2009; Kienle et al., 2022; Margot et al., 2013; Zimmermann et al., 2011). Because of their biodegradability, oxygen-rich compounds such as carbonyls and carboxylic acids are often summarized under assimilable organic carbon (AOC) or biodegradable organic carbon (BDOC). It has been shown in many studies that AOC and/or BDOC generally increases during oxidation processes (lower extent for chlorine and chlorine dioxide, (Ramseier et al., 2011; Swietlik et al., 2009)), with the strongest increase during ozonation (Hammes et al., 2007, 2006; Nawrocki et al., 2003; Swietlik et al., 2009; Van der Kooij et al., 1989). It has also been demonstrated in drinking water that the AOC/BDOC is abated in biological post-treatment leading to biologically stable water in distribution systems, which only requires minimal or no disinfectant residual (Gulde et al., 2021a; Hammes et al., 2006; Richardson et al., 1999a; Rosario-Ortiz et al., 2016). Another class of oxidatively induced DBPs comprises of *N*-nitrosamines, which are problematic mutagenic compounds, which can be formed during chloramination, chlorination and ozonation (Andrzejewski et al., 2008; Krasner, 2009; Krasner et al., 2018; Schmidt and Brauch, 2008; Shah and Mitch, 2012). *N*-Nitrosamines are biodegradable and also photolabile, which leads to their abatement in biological treatment and if exposed to sunlight/UV light (Bourgin et al., 2018; Plumlee and Reinhard, 2007; Schindler Wildhaber et al., 2015; Schmidt and Brauch, 2008; Stefan and Bolton, 2002; Zimmermann et al., 2011).

During chlorine-based oxidation processes (chlorine, chloramine), lesser extent for chlorine dioxide (partial chlorine formation from reaction with phenolic moieties in DOM) (Rougé et al., 2018; Terhalle et al., 2018) a whole suite of chlorinated, brominated and iodinated DBPs can be formed, such as trihalomethanes (THMs), halo acetic acids (HAAs), halo acetoneitriles (HANs), halo benzoquinones, etc. (Richardson and Ternes, 2022). Typically, the toxicity increases in the order chlor- < bromo- < iodo-compounds (Richardson et al., 2008; Stalter

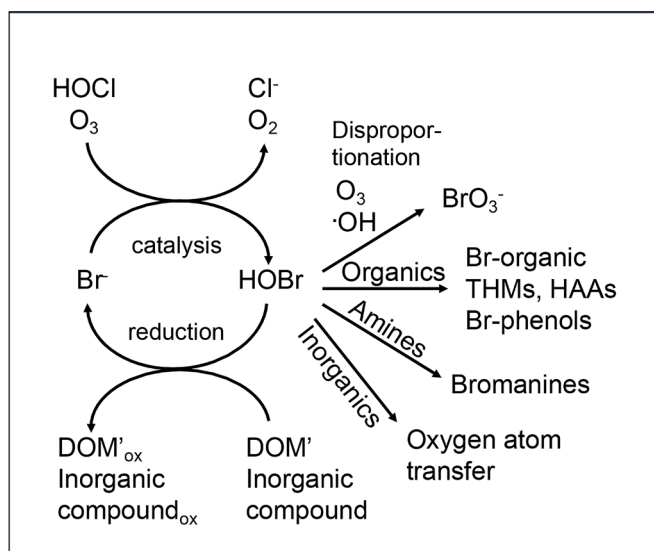


Fig. 10. Oxidation of bromide-containing waters and the ensuing reaction products.

et al., 2016; Yang et al., 2014) and therefore, the presence of bromide and iodide, which can be transformed to active bromine and iodine (Figs. 10, 11) has to be considered (Allard et al., 2015; Bichsel and von Gunten, 1999; Garland et al., 1980; Haag and Hoigné, 1983; Heeb et al., 2014; Kumar and Margerum, 1987; Nagy et al., 1988).

7.2. Role of bromide

Bromide plays a special role during oxidative water treatment (Fig. 10). It can act as a catalyst for oxidant consumption, triggered by organic (reacting by electron transfer, e.g., catechol, DOM isolates) (Criquet et al., 2015) and inorganic compounds (e.g. ammonium, Mn (II), HOI, IO_2^-) (Allard et al., 2013; Criquet et al., 2012; Haag et al., 1984; Heeb et al., 2014). Furthermore, HOBr which results from the oxidation of bromide can undergo reactions with aromatic and amine-type compounds (Acero et al., 2005; Criquet et al., 2015; Heeb et al., 2017). Non-conjugated olefins only have limited reactivity with HOBr, whereas conjugated olefins react with second-order rate constants of up to 10^3

$\text{M}^{-1}\text{s}^{-1}$ (Li et al., 2020a; Marron et al., 2021). During ozonation, reactions of activated aromatic compounds with HOBr are mostly inhibited because the ozone concentrations are typically higher and the HOBr-reactive compounds are already abated by ozone before HOBr reaches significant levels (Pinkernell and von Gunten, 2001). Therefore, the formation of Br-DBPs is only minor during ozonation of bromide-containing waters (Richardson et al., 1999b).

Because DBPs are often formed in minor side reactions, individual halogenated DBPs only account for part of the total organic halogen (TOX) and therefore, many important classes of compounds are still unknown but they may be crucial for the observed toxicity (Li and Mitch, 2018; Mitch et al., 2023; Stalter et al., 2020). Filling this gap and also selecting the toxicologically relevant DBPs for drinking water regulations is an active field of research (Li and Mitch, 2018).

7.3. Role of iodide

As discussed above, I-DBPs are more toxic than the Cl- and Br-analogous (Dong et al., 2019; Stalter et al., 2016). Therefore, the fate of iodine during oxidative processes is of special interest. Fig. 11a shows the oxidation of iodide by different oxidants to HOI, with the corresponding half-life times for the oxidants Fe(VI), O_3 , HOBr, HOCl, MnO_4^- , ClO_2 and NH_2Cl for a concentration of $10 \mu\text{M}$ (MacKeown et al., 2022). The oxidation of iodide is generally a fast process and HOI is readily formed by most commonly applied chemical oxidants with half-life times $< 100 \text{ s}$ (Fig. 11a, left). HOI is the critical intermediate which can react with DOM moieties to I-DBPs or be further oxidized to iodate (Bichsel and von Gunten, 1999), which is the desired form, because it does not form I-DBPs and is non-toxic (Bürgi et al., 2001). Iodate is readily formed by ferrate(VI), ozone and HOBr, but more slowly by HOCl, MnO_4^- and not or to a small extent by NH_2Cl and ClO_2 (Bichsel and von Gunten, 1999; Hua and Reckhow, 2007; Li et al., 2020b; Shin et al., 2018; Ye et al., 2013; Zhao et al., 2016). Iodate formation during application of ClO_2 might be due to chlorine formation from ClO_2 reactions with DOM (see above, (Rougé et al., 2018; Terhalle et al., 2018)). Therefore, the lifetime of HOI and the chance of formation of I-DBPs increases in the order $\text{Fe(VI)} < \text{O}_3 < \text{HOBr} < \text{HOCl/MnO}_4^- < \text{NH}_2\text{Cl/ClO}_2$ (Fig. 11a). Fig. 11a also shows the reduction of HOI by H_2O_2 , which is e.g. present in the AOP UV/ H_2O_2 . Even though hydroxyl radicals which are formed in this process can oxidize HOI to IO_3^- (Lin, 1980), the reduction of the intermediate HOI by H_2O_2 will lead back to iodide ($k_{\text{app, pH } 7.1} = 8.9 \times 10^3 \text{ M}^{-1}\text{s}^{-1}$, (Shin et al., 2020)). Therefore, iodine is not

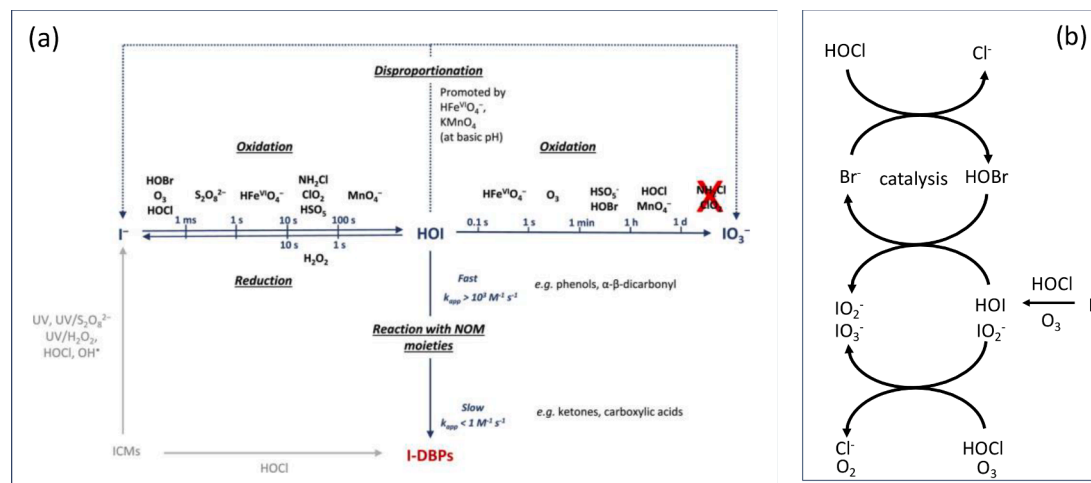


Fig. 11. Iodine in chemical oxidation processes. (a) Main reactions for the transformation of iodide to I-DBPs or iodate. The times indicated on the x-axis are half-lives for an oxidant/reductant concentration of $10 \mu\text{M}$. NH_2Cl and ClO_2 lead to very limited formation of iodate (probably caused by some free chlorine formed in these two processes). (b) Bromide-catalyzed oxidation of HOI to IO_3^- during chlorination of bromide- and iodide-containing waters. The iodate formation pathway is also shown for ozone, but there is no bromide-catalysis in this case because the direct ozone reactions are all very fast. (a) From (MacKeown et al., 2022), copyright Elsevier 2022.

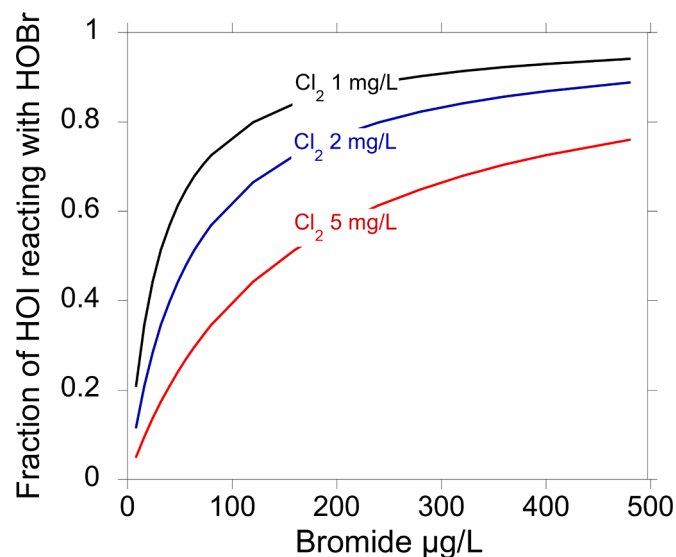


Fig. 12. Fraction of HOI reacting with HOBr as a function of the bromide concentration at pH ~7 for various chlorine concentrations (1–5 mg/L).

transformed to its non-problematic sink iodate in this process and the formation of iodo-organic compounds is possible during post-disinfection of such waters by chlorine or chloramine (Criquet et al., 2012; Shin et al., 2020). A special case is the enhanced iodate formation during chlorination of bromide- and iodide-containing waters (Fig. 11b). The direct oxidation of iodide to iodate by chlorine is quite slow (Fig. 11a) (Bichsel and von Gunten, 1999). In bromide-containing waters, HOBr is formed by reaction with HOCl ($k_{\text{HOCl,Br}} = 1550 \text{ M}^{-1}\text{s}^{-1}$, (Kumar and Margerum, 1987)), which reacts much faster with HOI compared to HOCl (pH 7: $k_{\text{appHOBr,HOI}} = 740 \text{ M}^{-1}\text{s}^{-1}$ (Criquet et al., 2012), $k_{\text{appHOCl,HOI}} = \sim 20 \text{ M}^{-1}\text{s}^{-1}$ (Bichsel and von Gunten, 1999)) to iodite and eventually iodate in a bromide-catalyzed reaction (Fig. 11b).

The fraction of HOI reacting with HOBr is shown in Fig. 12 for a variation of the bromide concentration and for three levels of chlorine. For a typical chlorine concentration of 1 mg/L and a bromide concentration of 50 µg/L, the fraction of HOI reacting HOBr is about 60%. For a higher chlorine concentration of 5 mg/L, the fraction of the HOI reacting with HOBr at 50 µg/L bromide decreases to about 20%. The fraction of HOI reacting with HOBr for a bromide concentration of 200 µg/L increases to ~90% and ~60% for chlorine concentrations of 1 and 5 mg/L, respectively.

7.4. Inorganic compounds

During application of chemicals for water treatment, some inorganic DBPs may be formed, including chlorite, chlorate, bromate and iodate (see above). Chlorite and chlorate are potential blood toxins and are the main DBPs from the application of chlorine dioxide and mainly formed from its reactions with DOM (Abdighahroudi et al., 2021; Schmidt et al., 2000; WHO, 2017). Chlorite accounts for about > 50% of the chlorine dioxide dose and since it is regulated in drinking water, it often limits the applicable doses of chlorine dioxide (Houska et al., 2021; Hupperich et al., 2020; Schmidt et al., 2000). Chlorate is also formed in bleach by disproportionation and is added to waters by dosing of chlorine solutions with median concentrations of 110 µg/L for a chlorine dose of 1 mg/L as was demonstrated previously (Bolyard et al., 1992).

Bromate is formed during ozonation of bromide-containing waters by a complex mechanism including both ozone and $\cdot\text{OH}$ reactions. Bromate is a possible human carcinogen and is regulated at 10 µg/L in drinking water; its formation is often the limiting factor for ozone applications (Morrison et al., 2023). Understanding the bromate formation mechanism was crucial to develop mitigation strategies to minimize its

formation (Buffle et al., 2004; Krasner et al., 1993; Morrison et al., 2023; Pinkernell and von Gunten, 2001; Song et al., 1996, 1997; von Gunten, 2003; von Gunten and Hoigné, 1994; von Gunten and Oliveras, 1998; von Sonntag and von Gunten, 2012). Some of the mitigation strategies for bromate include quenching of bromide by pre-oxidation with chlorine followed by ammonium addition (Buffle et al., 2004; Neemann et al., 2004), reduction of HOBr by H_2O_2 (von Gunten and Oliveras, 1997; 1998), quenching of HOBr by NH_3 (Haag et al., 1984; Heeb et al., 2017) and quenching of bromine radicals by DOM and/or NH_2Cl (Lei et al., 2022; Lim et al., 2023). Such approaches can reduce bromate formation by up to 90%, however, they have to be adapted to the specific treatment goals and the water quality. Post-treatment is not a viable option in this case, because in contrast to other oxygen-rich organic DBPs, bromate is not abated during aerobic biological post-treatment nor well adsorbed on (biological) activated carbon (Bao et al., 1999; Hijnen et al., 1995; Kirisits et al., 2001; Kruthof et al., 1993).

Bromate is also a potential problem in chlorinated systems: It can be formed in concentrated bleach solutions containing bromide by disproportionation of the formed bromine (Beckwith and Margerum, 1997) and upon chlorine dosage, bromate is also added to the water (Weinberg et al., 2003). In a survey in the US it was shown that $\leq 3 \mu\text{g/L}$ of bromate are added to drinking water by this route (Weinberg et al., 2003). This might be an issue for utilities using an ozonation prior to chlorination and reduce their range of operation. A second possibility is bromate and also minor chlorate formation during chlorination of waters with copper pipes in presence or absence of bromide, respectively (Liu et al., 2012). CuO , a corrosion product of copper pipes can catalyze the disproportionation of hypohalous acids (Gray et al., 1977; Liu et al., 2012) and this has been mainly demonstrated in distribution systems after desalination (Alomirah et al., 2020).

Finally, bromate can also be formed during ferrate(VI)-based processes of bromide-containing waters. Its formation is typically slow and enhanced at pH < 7. It has been shown that the formation of hydrogen peroxide during the decay of ferrate(VI) (Lee et al., 2014) plays a crucial role in the extent of bromate formation. In presence of phosphate buffer the concentration/lifetime of hydrogen peroxide increases and therefore, the bromate formation is reduced (Huang et al., 2016; Jiang et al., 2016). However, under realistic conditions, phosphate concentrations are typically low, which may lead to some bromate formation.

8. Conclusions and outlook

The application of chemical oxidants for micropollutant abatement in water treatment requires an assessment of several aspects such as reaction kinetics, formation of transformation products, toxicity/biological activity of transformation products, biodegradability of transformation products relative to the target compounds, reaction with water matrix components such as dissolved organic matter, bromide and iodide. In the last 30+ years, I participated in research efforts, which led to a better understanding of all these factors by collaborations among different disciplines, including environmental, physical and analytical chemistry, environmental toxicology, environmental microbiology and environmental engineering. Furthermore, collaborations with practitioners from the water and wastewater sector led to a significantly better understanding of realistic and relevant scenario and to many new research questions. Based on this, the current knowhow allows theoretical assessments of the feasibility of oxidation processes for a given real-world situation. Experimental tests including some or all of the above aspects may still be required to design and implement a treatment system. There have also been significant efforts and success to combine experimental research for abatement of micropollutants with *in silico* approaches including prediction of reaction rate constants and reaction mechanisms, toxicity and biodegradability. In the future, this successful approach will be further developed and will also enable a better control of inorganic and organic disinfection byproducts.

CRedit authorship contribution statement

Urs von Gunten: Conceptualization, Data curation, Methodology, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The author declares that he has no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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