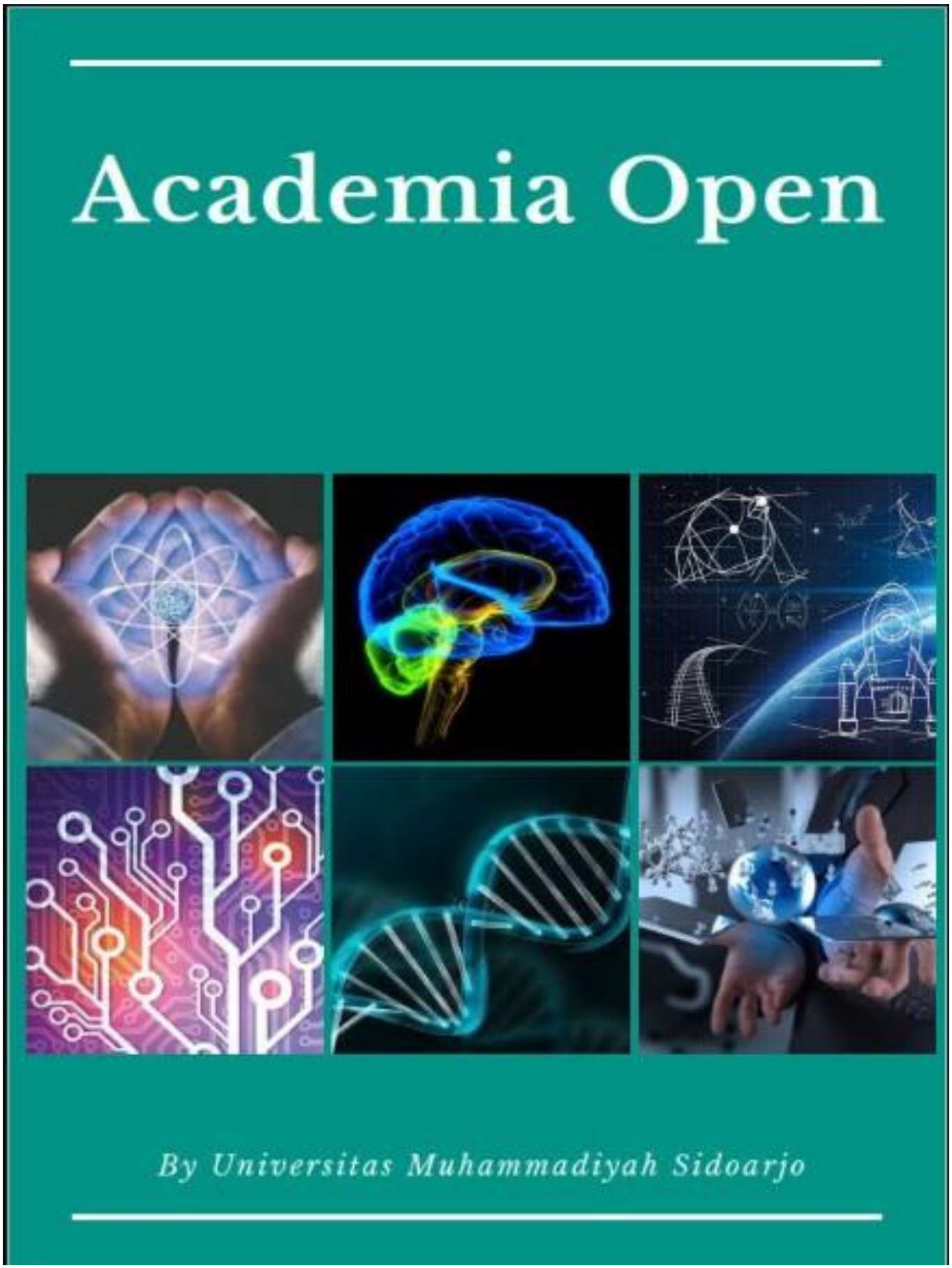
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Artificial Intelligence Framework Predicts Residual Ecotoxicity During Advanced Oxidation Water Treatment

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Abstract

General Background Advanced oxidation processes (AOPs) efficientlydegradestructurallyresistant contaminants of emerging concern (CECs) in tertiary wastewater treatment. **Specific Background** Conventional performance metrics rely on the disappearance of the parent compound, ignoring the formation of transformation products (TPs) whose persistence, mobility, and toxicity often exceed those of the parent structure. **Knowledge Gap** Current targeted analytical workflows frequently leave transient TPs undetected, and existing predictive models lack a cohesive, validated framework that integrates radical reactivity, in silico enumeration, and toxicity predictions to actively manage residual risk. **Aims** This critical review evaluates the mechanistic origins of toxic TPs and proposes a conceptual tiered framework that couples density functional theory (DFT) reactivity descriptors, graph neural networks (GNNs), high-resolution mass spectrometry (HRMS), and machine-learning toxicity predictions into a mixture-aware Net Ecotoxicity Index (NEI). **Results** Radical-mediated electrophilic addition, single-electron transfer, and hydrogen abstraction generate reactive electrophiles and halogenated or nitrated TPs that significantly raise residual mixture toxicity. The proposed AI-assisted framework integrates these chemical pathways to predict TP formation and structure, prioritizing analytical screening through HRMS, and subsequently assessing ecotoxicity using QSAR models to inform supervisory oxidant dosing. **Novelty** This framework shifts the AOP control paradigm from parent-compound degradation tracking to prospective, AI-driven residual ecotoxicity prediction and mitigation. **Implications** Adopting mixture-aware predictive control strategies requires establishing open TP datasets, applying precise applicability domains in modeling, and shifting regulatory targets toward effect-based risk assessments.

Highlights:

- Evaluating advanced oxidation performance solely by parent compound degradation masks the potential toxicity of transformation products.
- Integrating DFT descriptors and graph neural networks enables the prospective in silico identification of toxic transformation products.

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- AI-assisted toxicity predictions integrated with HRMS screening can dynamically control oxidant dosing to minimize residual ecotoxicity.

Keywords: Advanced Oxidation Processes, Residual Ecotoxicity, Transformation Products, Machine Learning, Net Ecotoxicity Index

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1. Introduction

1.1 Contaminants of emerging concern and the treatment gap

Contaminants of emerging concern (CECs), including pharmaceuticals, endocrine-disrupting chemicals, personal-care ingredients, pesticides and per- and polyfluoroalkyl substances (PFAS), reach aquatic systems largely through municipal and industrial effluents, because conventional activated-sludge treatment was not designed to remove them [1]. Their polarity, limited biodegradability and low concentrations (ng L−1 to μg L−1) make removal by coagulation, sedimentation or sand filtration inefficient, which has driven the uptake of tertiary processes [2].

1.2 Advanced oxidation processes and their reactive species

AOPs generate highly oxidative radicals in situ, mainly •OH, and increasingly SO4•−, which attack organic structures resistant to biological and physical treatment [3], [4]. Typical setups include ozonation (O3, O3/H2O2), UV/H2O2, Fenton and photo-Fenton, UV- or catalyst-activated persulfate and peroxymonosulfate, and heterogeneous photocatalysis [5]–[7]. Table 1 compares the properties important for TP formation: •OH reacts with most organic molecules at near diffusion-controlled rates and is therefore weakly selective, while SO4•− and molecular ozone are more selective for electron-rich moieties [8]–[11].

Table 1. Properties of the principal reactive species in AOPs relevant to transformation product (TP) formation.

Species	Standard reduction potential (E°)	Typical second-order rate constants with organics	Selectivity and dominant mode of attack	Key sources
Hydroxyl radical (•OH)	≈2.7–2.8 V at pH 0; ≈1.9 V at pH 7	10^8–10^{10} M^{-1} s^{-1}	Low selectivity; radical addition to C=C and aromatic rings, H-atom abstraction	[8], [12]
Sulfate radical ($SO_4^{\bullet-}$)	≈2.5–3.1 V (pH-dependent)	10^6–10^{10} M^{-1} s^{-1}	Higher selectivity for electron-rich aromatics; single-electron transfer; also addition and H-abstraction	[9], [11]
Molecular ozone (O_3)	≈2.07 V (acidic)	<1 to >10^6 M^{-1} s^{-1}	Selective: amines, olefins, activated aromatics, phenolates; Criegee-type ring cleavage	[10]
Reactive halogen species (Cl•, $Cl_2^{\bullet-}$, Br•)	≈2.4 V ($Cl^{\bullet}/Cl^-$); lower for $Cl_2^{\bullet-}$	Substrate dependent; often 10^8–10^{10} M^{-1} s^{-1}	Formed when •OH or $SO_4^{\bullet-}$ oxidize Cl^-/Br^-; electrophilic halogenation and electron transfer	[12], [13]
Hydrated electron (e_{aq}^-)	≈−2.9 V	Up to ~10^{10} M^{-1} s^{-1} with electron-deficient substrates	Reductive; hydrogen/fluorine exchange; relevant to advanced reduction of PFAS	[8], [14]

Values are indicative ranges; matrix composition and pH shift effective rates. E° values refer to aqueous solution versus the standard hydrogen electrode.

1.3 The degradation–mineralization paradox

Complete mineralization turns carbon into CO2, water and inorganic ions:

Organic contaminant + ROS/RSS → n CO2 + m H2O. X X− (1)

In practice mineralizing trace contaminants in complex effluent is rarely economical because oxidant is used up by the water matrix and reaction rates slow when more reactive intermediates are made. The electrical energy per order abbreviated as EEO is the energy needed to drop a concentration by one order of magnitude in a unit volume and it is the standard figure of merit [15]:

EEO = (P • t • 1000) / (V • 60 • log(Ci/Cf)) (2)

Here P stands for the power in kilowatts t is the irradiation or treatment time in minutes V is the treated volume in litres and Ci and Cf are the final concentrations. Because EEO is defined for the parent compound it rewards the disappearance of the compound. Does not notice what is formed. Therefore processes are run with less, than the stoichiometric amount of oxidant. Leave behind a mixture of partially oxidized transformation products (TPs). The composition of this mixture depends on the oxidant, the matrix and the dose [10], [16].

1.4 Aim and scope

This is a narrative critical review and not a systematic review. Sources were selected for mechanistic relevance and for studies that combined chemical identification of TPs with assessment of biological or modeled effects. Quantitative toxicity

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values are reported only where we could confirm them in the primary or an authoritative secondary source. The review (i) examines the evidence that parent removal is an unreliable proxy for safety, (ii) explains the radical-chemistry origin of toxic TPs, (iii) evaluates the analytical blind spot, and (iv) proposes and critically bounds a computational–analytical framework for TP-aware process control.

2. The "Disappearance" Paradigm and Its Limits

2.1 Metrics used to judge AOP performance

Performance is conventionally expressed as parent removal efficiency,

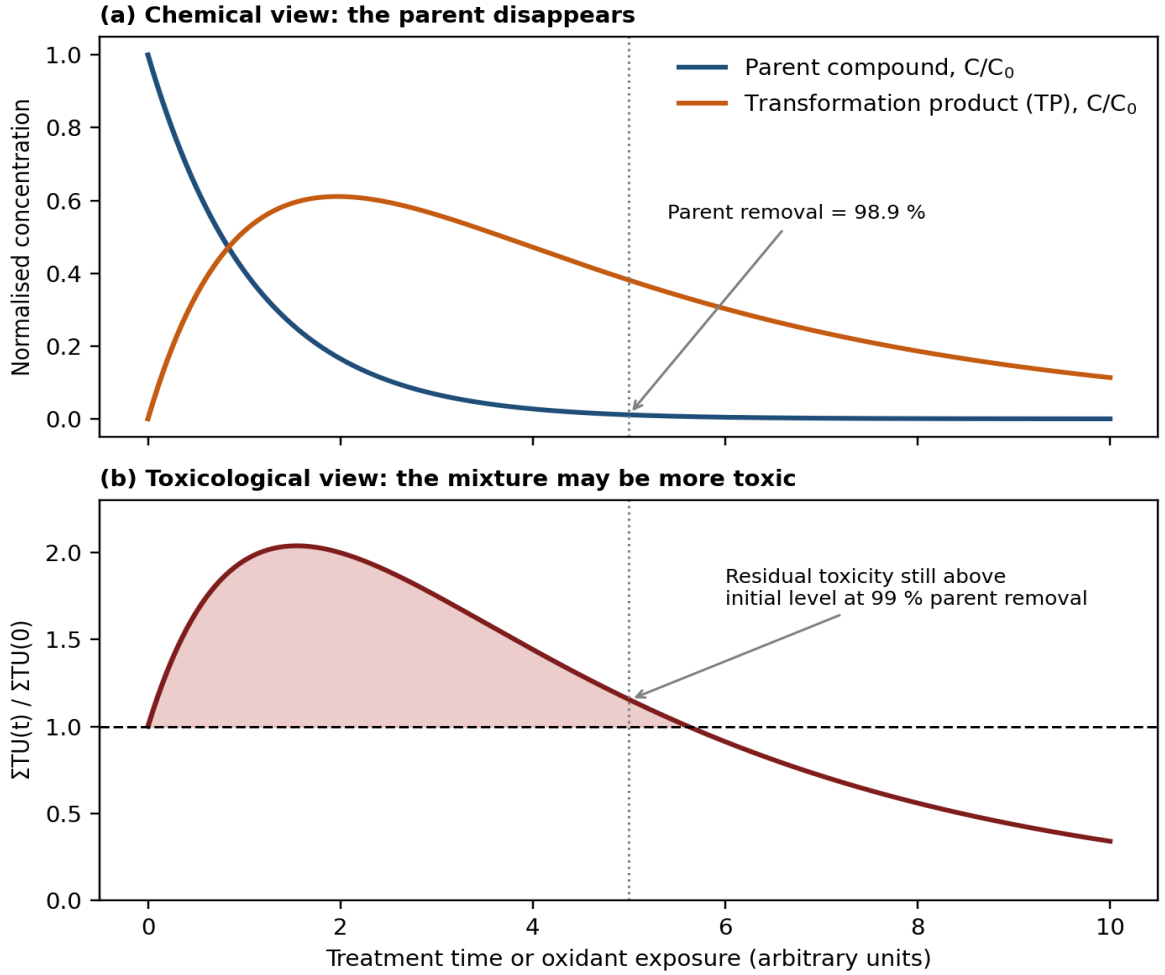
$$\eta_{parent} = [(C_0 - C_t) / C_0] \times 100\ \% \quad (3)$$

with C0 and Ct the parent concentrations at time zero and time t. Mineralization is sometimes added as ηTOC:

$$\eta_{TOC} = [(TOC_0 - TOC_t) / TOC_0] \times 100\ \% \quad (4)$$

Neither metric reports toxicity. A high ηparent can coexist with a low ηTOC and a mixture of TPs of unknown effect, so a toxicity-oriented metric is required (Section 5.5). Conceptually, Fig. 1 shows that the sum of toxic units of the mixture can be greater than the initial value even if the parent has essentially disappeared if a TP is formed faster than it is degraded and is more potent per unit concentration than the parent.

Figure 1. Conceptual illustration of the "vanish" paradigm. (a) Sequential first order kinetics for parent compound and one intermediate. (b) Relative summed toxic units vs. initial value. Parameters for illustration; figure is not experimental data.



Conceptual simulation (sequential first-order kinetics, $k_1 = 0.9$, $k_2 = 0.25$; TP assumed 3 times more toxic per unit concentration). Not experimental data.

2.2 Empirical evidence that removal and safety can diverge

The literature focused on effects is more complex than just a straightforward "oxidation leads to toxicity" story, and an even interpretation is crucial. A systematic review of in vitro and in vivo studies found that enhancing wastewater treatment with ozonation or activated carbon typically boosts toxicity removal; however, ozonation produces harmful TPs that can be

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eliminated through post-treatment [17]. Comparable conclusions emerged from a critical assessment of chemical and biological evaluation of treatment technologies [18] and from studies showing that targeted chemical analysis and (geno)toxicity assessment can tell different stories about the same treatment [19]. Recently, a risk-driven comparison of ozone and granular activated carbon used PNEC-based risk for 20 pharmaceuticals and QSAR predictions for their oxidation TPs: parent-based risk fell by a median of 73 % with ozone, but when predicted TP toxicity was included the median risk reduction became negative (−274 ± 124 %), indicating a modelled increase in risk [20]. Because the TP toxicities in that study were QSAR-estimated, the result should be read as a hypothesis-generating signal and not as proof, which is precisely why validated TP-aware predictive tools are needed.

Compound-level studies show how the divergence arises (Table 2). In the photodegradation of diclofenac, effect-directed analysis identified 2-[(2-chlorophenyl)amino]benzaldehyde as a TP with an EC50 toward the green alga Scenedesmus vacuolatus of 4.8 mg L−1, about tenfold lower than that of diclofenac (48.1 mg L−1), a difference attributed to its higher hydrophobicity (log Kow 3.62 versus log Dow 2.04 at pH 7) [21]. More recent work on photolytic and photocatalytic treatment reports that the persistent diclofenac TPs are mainly carbazole derivatives with toxicity and persistence comparable to the parent [22], which illustrates that TP hazard is pathway- and condition-specific. During ozonation of sulfamethoxazole, acute toxicity toward Daphnia was reported to rise in the early stages of reaction and considerable toxicity persisted after the antibiotic was fully depleted [23].

Table 2. Selected documented cases in which parent-compound removal and residual toxicity or risk diverge (or where TP behaviour determines the outcome).

Contaminant / system	Treatment	TPs or by-products highlighted	Effect or risk observation	Source
Diclofenac (NSAID)	Photolysis / photo-transformation	2-[(2-Chlorophenyl)amino]benzaldehyde; carbazole derivatives	Aldehyde TP: EC_{50} (*S. vacuolatus*) 4.8 mg L^{-1} versus 48.1 mg L^{-1} for the parent; later work: carbazole TPs with comparable toxicity and persistence	[21], [22], [24]
Sulfamethoxazole (antibiotic)	Ozonation (aqueous solution)	Partially oxidized by-products (identified by LC–MS)	Acute toxicity (*Daphnia*) elevated during early reaction; considerable toxicity persisted after parent depletion	[23]
20 (psycho)pharmaceuticals in effluent	Ozone versus granular activated carbon	Oxidation TPs (QSAR-predicted)	Parent-based median risk reduction 73 % (ozone); median risk reduction −274 ± 124 % when predicted TP toxicity included	[20]
Municipal effluent micropollutants	Ozonation with post-treatments (sand filtration, GAC, biological)	Ozonation TPs detected by non-target screening	54–83 % of non-target features formed by ozonation were removed in post-treatment, with GAC filters performing best	[25]–[27]
Effluent toxicity (in vitro and in vivo, many studies)	Ozonation or activated carbon	Mixture of OTPs	Overall toxicity removal improves, but toxic OTPs form and are removable by post-treatment	[17], [18]
Bromide-containing waters	Ozonation	Bromate and brominated by-products	Inorganic and organic oxidation by-products arise independently of parent removal	[28]

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PFOA / PFOS	Reductive and plasma-based processes	Shorter-chain perfluoroalkyl species	Defluorination is structure dependent and incomplete; shorter-chain products remain persistent	[14], [29]

Quantitative values are reproduced only where verified in the cited source. OTP, oxidation transformation product; NSAID, non-steroidal anti-inflammatory drug.

2.3 Chemical mechanisms that can raise TP hazard

Five different chemical pathways are consistently referenced (Table 3). Initially, hydroxylation of the •OH ring followed by oxidation produces quinones, and after the ring opens, it forms unsaturated dicarbonyls; these mild electrophiles interact covalently with nucleophilic sites in proteins and DNA through Michael addition [30], [31]. Secondly, a structural alteration like cyclization or the removal of a polar group can increase hydrophobicity and thereby baseline toxicity, similar to the diclofenac case mentioned earlier. Third, in matrices with halides, •OH and SO4•− oxidize Cl− and Br− into reactive halogen species, affecting degradation rates and generating halogenated products [13], [32], whereas ozonation of bromide results in bromate [28]. Fourth, nitro- and nitroso-aromatics, which can result from the oxidation of aromatic amines or from radical nitration in the presence of nitrate or nitrite, are problematic for mutagenicity [33]. Ultimately, oxidation at sites distant from a pharmacophore can preserve the mode of action, which underpins the read-across from parent to TP in risk evaluation [34].

Table 3. Mechanistic drivers of increased or retained hazard in TPs and their implications for monitoring.

Driver	Chemical origin in AOPs	Evidence base	Monitoring implication
Reactive electrophiles (quinones, α,β-unsaturated carbonyls)	•OH ring hydroxylation, oxidation to quinones, ring opening	[30], [31]	Include electrophile-sensitive and oxidative-stress bioassays; carbonyl-targeted non-target workflows
Higher hydrophobicity / membrane partitioning	Cyclization, loss of polar substituents	[21]	Use log *D*-dependent baseline-toxicity QSARs for each TP
Halogenated TPs and by-products	Halide oxidation to Cl•, $Cl_2^{\bullet-}$, Br•; HOBr formation in ozonation	[13], [28], [32]	Treat halide concentration as a model input; monitor bromate
Nitro / nitroso aromatics	Oxidation of aromatic amines; radical nitration with NO_2• in nitrate/nitrite matrices	[33]	Genotoxicity screening (e.g., Ames-type) alongside chemical analysis
Retained mode of action	Oxidation distant from the pharmacophore	[34]	Apply parent-to-TP read-across with structural-similarity thresholds
Persistent small or short-chain products	Incomplete oxidation or reduction	[14], [29]	Add short-chain and polar-product methods (e.g., HILIC); consider post-treatment

2.4 Analytical blind spots

Targeted LC–MS/MS requires reference standards, which rarely exist for short-lived or rare TPs, so these compounds are not quantified. Suspect and non-target screening with HRMS (Q-TOF, Orbitrap) can detect unknown masses, but identification remains the bottleneck [35]–[37]. Reporting the confidence of each identification is essential to interpret TP risk [38] (Table 4). Non-target workflows have nonetheless proved decisive for tracing ozonation TPs through treatment trains, for example by distinguishing features that are formed by ozonation and subsequently removed [25], [26].

Table 4. Identification confidence levels for HRMS-derived features and their use in TP risk assessment.

Level	Definition [38]	Suggested use in TP-aware risk assessment
1	Confirmed structure (match with reference standard: MS, MS/MS, retention time)	Quantify; apply measured toxicity data where available
2	Probable structure (library spectrum match, 2a; or diagnostic evidence, 2b)	Semi-quantify; apply QSAR/read-across with narrow applicability domain
3	Tentative candidate(s) (structure class or isomer set)	Use worst-case or class-based predictions across candidates
4	Unequivocal molecular formula	Report as feature; prioritize by intensity trend; include in effect-based testing
5	Exact mass of interest	Track trend only; escalate if associated with measured effect

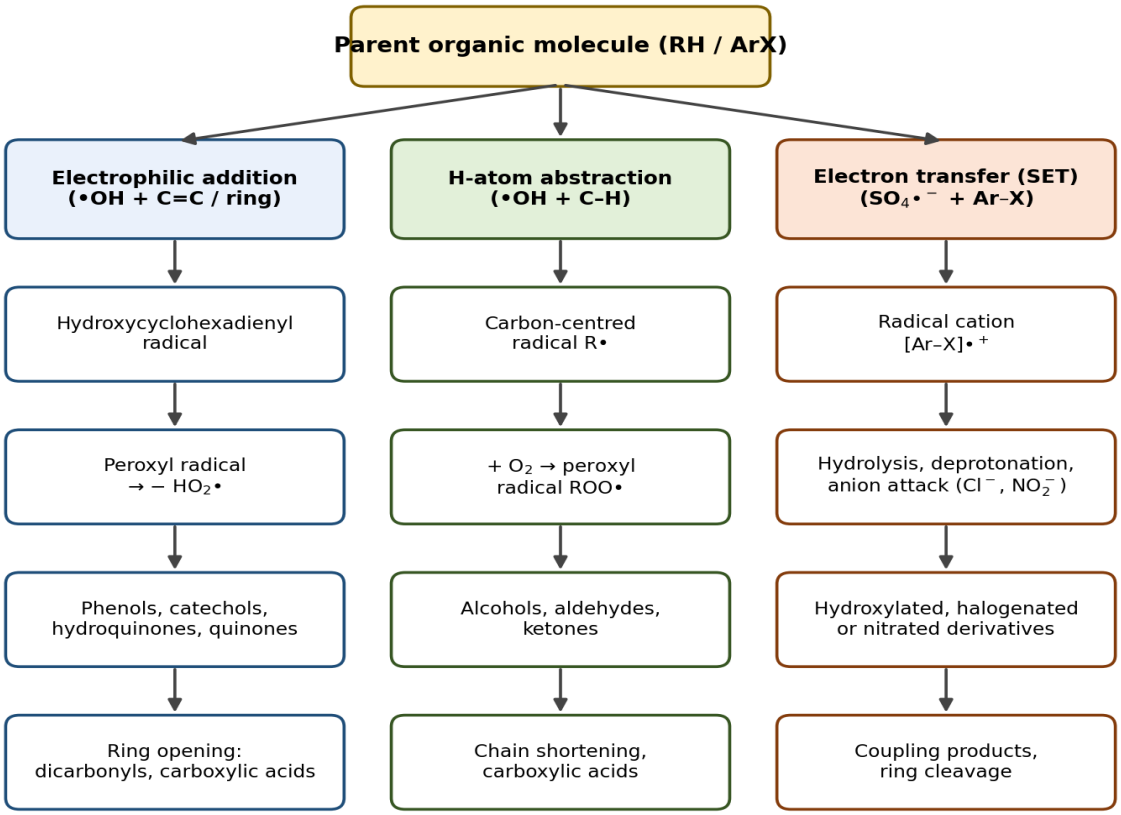
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3. Mechanistic Pathways of Radical Attack and TP Genesis

Three elementary routes account for most TP formation (Fig. 2): radical addition, hydrogen-atom abstraction and single-electron transfer [7], [10].

Figure 2. Principal radical-mediated routes to transformation products. Pathway selection depends on the oxidant, substrate structure and water matrix.



Competing pathways yield TP mixtures whose composition depends on oxidant, matrix (halides, nitrate, organic matter) and dose

3.1 Electrophilic addition to aromatic rings

•OH adds to C=C bonds and aromatic rings at near diffusion-controlled rates to form a hydroxycyclohexadienyl radical, which in the presence of dissolved O2 adds oxygen and then eliminates HO2• to yield hydroxylated aromatics (phenols, catechols, hydroquinones):

$$ArH + \bullet OH \rightarrow [HO–ArH]\bullet \quad (5)$$

$$[HO–ArH]\bullet + O_2 \rightarrow [HO–ArH–OO]\bullet \rightarrow ArOH + HO_2\bullet \quad (6)$$

Further oxidation breaks aromaticity and gives aliphatic dicarbonyls and carboxylic acids.

3.2 Hydrogen-atom abstraction

For saturated moieties, •OH abstracts a hydrogen atom, and the carbon-centred radical combines rapidly with O_2 (rate constants of the order of 10^9 M^{-1} s^{-1}):

$$R–H + \bullet OH \rightarrow R\bullet + H_2O \quad (7)$$

$$R\bullet + O_2 \rightarrow ROO\bullet \quad (8)$$

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Peroxyl radicals undergo bimolecular decay or unimolecular elimination to give carbonyl compounds and alcohols, which are the commonly observed stable intermediates [10].

3.3 Single-electron transfer

$SO_4^{\bullet-}$ reacts with electron-rich substrates mainly by electron transfer to produce radical cations ($SO_4^{\bullet-}$ may also add to double bonds or abstract hydrogen):

$$Ar–X + SO_4^{\bullet-} \rightarrow [Ar–X]^{\bullet+} + SO_4^{2-} \quad (9)$$

The radical cation can undergo hydrolysis, deprotonation or attack by ambient anions (e.g., Cl−, NO2−), which steers the system toward product distributions different from those of •OH [7], [11]. In chloride-containing waters, sulfate-radical oxidation of phenolic compounds yields chlorinated products [32].

Note on nitration. Reports of nitro-derivatives of pharmaceuticals during ozonation should not be attributed to reactive nitrogen species by default; oxidation of an aromatic amine to its nitroso and nitro analogue is an alternative route that does not require nitrate or nitrite. Mechanistic assignment should therefore be supported by labelling or scavenger experiments.

4. Water-Matrix Effects on TP Genesis

Effluent organic matter (EfOM) competes for radicals and may modify TP distributions [39], while halides, carbonate and nitrate alter the radical pool and introduce secondary species [13]. Any predictive model that ignores these co-variates will extrapolate poorly from pure-water experiments to real effluents; the matrix descriptors in Stage 1 of the proposed framework (Section 5.1) exist for this reason. Post-treatment also influences the final hazard: biological or sorptive steps remove a large fraction of ozonation TPs [25]–[27], so the relevant decision unit is the treatment train and not the AOP alone.

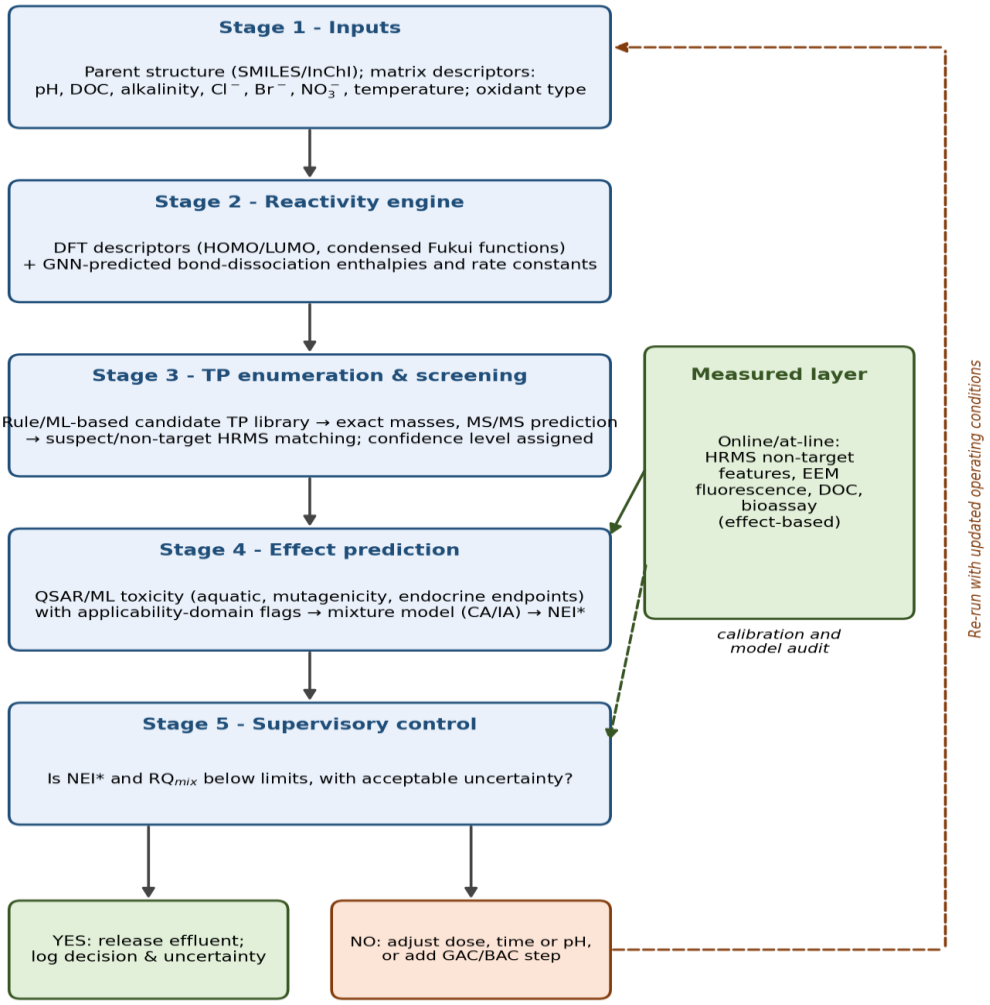
5. Proposed Framework: AI-Assisted TP Prediction and Ecotoxicity-Aware Control

We propose an integrated AI–AOP framework (Fig. 3) that combines quantum-chemical descriptors, machine learning, HRMS screening and toxicity prediction to anticipate TP formation and residual effect, and to inform supervisory control. The framework is conceptual: its components exist individually, but their integration for AOP control has not been experimentally validated. Table 5 summarizes the toolbox and the principal limitation of each component, and Table 6 proposes a staged validation roadmap.

Figure 3. Proposed five-stage AI–AOP framework with a measured layer for calibration and a feedback loop for supervisory control. NEI*, normalized Net Ecotoxicity Index; RQmix, mixture risk quotient; CA/IA, concentration addition/independent action; GAC/BAC, granular activated carbon/biological activated carbon.

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5.1 Stage 1: Molecular and matrix inputs

The parent structure is encoded as a canonical SMILES or InChI string. Matrix descriptors (pH, dissolved organic carbon, alkalinity, Cl−, Br−, NO3−, temperature) and the oxidant type and dose are co-variables, because they determine which reactive species dominate.

5.2 Stage 2: Reactivity engine

DFT calculations (for instance the B3LYP functional [40], [41]) provide frontier-orbital energies and condensed Fukui functions that indicate local susceptibility to electrophilic, nucleophilic or radical attack [42]. Using atomic electron populations Pk of atom k in the N-, (N+1)- and (N−1)-electron systems:

$$f_k^+ = P_k(N+1) - P_k(N) \quad \text{(nucleophilic attack)} \tag{10}$$

$$f_k^- = P_k(N) - P_k(N-1) \quad \text{(electrophilic attack)} \tag{11}$$

$$f_k^0 = [P_k(N+1) - P_k(N-1)] / 2 \quad \text{(radical attack)} \tag{12}$$

If atomic net charges qk are used instead, the signs reverse, and fk0 = [qk(N−1) − qk(N+1)] / 2. Fukui indices are a first-order guide to regioselectivity; they do not capture solvent effects, reaction barriers or the low regioselectivity of •OH addition, and should be complemented by bond-dissociation enthalpies and, where feasible, transition-state calculations. Graph neural networks trained on large DFT-derived datasets can predict homolytic bond-dissociation enthalpies at near-DFT accuracy with sub-second cost ([43]); the published model covers molecules containing C, H, N and O, so halogen- or sulfur-containing contaminants fall outside its domain and require retraining. Message-passing architectures for molecular property prediction are well established [44], and machine-learning models for •OH rate constants have been reported [45].

5.3 Stage 3: In silico TP enumeration and HRMS screening

Predicted radical-attack sites are combined with curated transformation rules (hydroxylation, dealkylation, ring cleavage,

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halogenation, nitration) to generate a candidate TP library. Rule-based and machine-learning predictors developed for biotransformation, such as the EAWAG pathway system, enviPath and BioTransformer, provide architectures that can be adapted, but abiotic oxidation rule sets must be curated [46]–[48]. Candidate masses then drive suspect screening and mass-defect-based prioritization of non-target HRMS data, with each feature assigned a confidence level [38]. By restricting the search space, such libraries are expected to shorten identification; the magnitude of this gain has not been benchmarked and should not be assumed.

5.4 Stage 4: Effect prediction

Candidate and identified TPs are passed to QSAR and machine-learning models for aquatic endpoints (e.g., fish, daphnid and algal toxicity), mutagenicity and endocrine activity, using freely available tools such as US EPA T.E.S.T. and ECOSAR or deep-learning classifiers such as DeepTox [49]. Reliability depends on adherence to good modelling practice and explicit applicability-domain assessment [50], [51]. A recognized weakness is that training sets are dominated by stable commercial chemicals rather than transient intermediates, so predictions for TPs must carry uncertainty bounds and domain flags [52].

Table 5. Computational and analytical toolbox for the proposed framework, with principal limitations.

Module	Representative method or tool	Output	Principal limitation	Key sources
Quantum-chemical reactivity	DFT (B3LYP) with condensed Fukui functions	Site reactivity indices; frontier orbitals	Computational cost; population-scheme dependence; no barriers or solvation by default	[40]–[42]
Bond-dissociation energies	Graph neural network trained on DFT data	Homolytic BDE per bond	Domain limited to C, H, N, O molecules in published model	[43]
Molecular property learning	Directed message-passing networks	Rate constants, properties	Needs curated AOP-specific data; interpretability	[44], [45]
TP enumeration	EAWAG-PPS, enviPath, BioTransformer (adapted)	Candidate TP libraries	Built for biotransformation; abiotic rules must be added	[46]–[48]
Analytical identification	LC–HRMS suspect and non-target screening	Annotated features with confidence levels	Identification bottleneck; ionization bias	[35]–[38]
Toxicity prediction	QSAR/ML (T.E.S.T., ECOSAR, DeepTox)	LC_{50}/EC_{50}, mutagenicity classes	Training bias toward stable parents; applicability domain	[49]–[51]
Mixture assessment	Concentration addition / independent action	Mixture toxic units or risk quotient	Assumes known concentrations and modes of action	[53]
Empirical verification	Effect-directed analysis; effect-based bioassays	Measured effect; causative features	Throughput; matrix interference	[18], [54]
Online surrogates	3D excitation–emission fluorescence (EEM)	Real-time matrix and EfOM indicators	Indirect link to TP toxicity	[55]

5.5 Stage 5: Net Ecotoxicity Index and supervisory control

The mixture effect is represented by concentration addition as the total of toxic units (TU = Ci/EC50,i), where Ci,t denotes the (measured or estimated) concentration of compound i at time t, and EC50,i is its median effective concentration for a specified species and endpoint [53]:

Since absolute values rely on the selected endpoint, the index is adjusted to the untreated effluent:

$$NEI^{*}t = NEIt / NEI0 \quad (14)$$

with the parent factored into the total at t = 0. When predicted no-effect concentrations exist, a mixture risk quotient may be utilized simultaneously:

$$RQmix,t = \Sigma i=1n (Ci,t / PNECi) \quad (15)$$

NEI* exceeding 1 indicates that the treatment has raised estimated toxicity, while RQmix over 1 indicates intolerable estimated risk. Three design principles are proposed. (i) In silico predictions should be supported by a measured layer (bulk bioassays, non-target feature patterns, and surrogate sensors), since unidentified TPs are excluded from the total. (ii) Decisions should be based on applicability-domain flags and uncertainty intervals, opting for caution when a TP is outside the model domain. (iii) Potential control measures should involve increasing contact time or dosage, modifying pH, and

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incorporating biological or GAC post-treatment, which evidence indicates significantly eliminates a large portion of ozonation TPs [17], [25], [26]. Increasing the oxidant dosage does not always have positive effects: it can push intermediates toward low-toxicity acids, but may also create additional by-products like bromate in water that contains bromide [28].

5.6 Validation roadmap

Table 6. Proposed tiered validation roadmap for the AI–AOP framework.

Tier	System	Benchmark	Suggested performance metrics
T0	Retrospective in silico benchmark	Curated literature sets of experimentally confirmed TPs and toxicities	Top-*k* recall of confirmed TPs; calibration of toxicity predictions; applicability-domain coverage
T1	Pure water, single compounds, bench scale	Targeted and non-target HRMS; standards where available	Precision/recall of predicted TP masses; rank correlation of predicted versus measured TP formation
T2	Spiked real effluent, bench scale	HRMS plus effect-based bioassays	Agreement of predicted NEI* with measured effect; false-negative rate for high-toxicity TPs
T3	Pilot plant with online surrogates	Online EEM, DOC, periodic HRMS and bioassay	Decision accuracy of control actions; response time; robustness to matrix variability
T4	Full-scale, longitudinal	Compliance-grade monitoring	Residual-effect reduction versus conventional control; operating cost; reproducibility across sites

Acceptance thresholds should be pre-registered before testing.

6. Challenges and Research Priorities

Achieving TP-aware AOP control depends on advancements in five domains (Table 7). The primary and most constraining factor is data: there is a lack of open, curated datasets that link AOP-generated TP structures, spectra, and toxicity, leading to biased machine-learning models [52]. Second, matrix complexity (EfOM, halides, carbonate, nitrate) should be depicted, not averaged. Third, mixture effects necessitate clear models, and any index derived from concentration addition must be evaluated against observed mixture responses [53]. Fourth, regulatory practices should shift from concentration-focused removal goals to targets based on effects or risks, as previously suggested by risk-oriented research [20]. Fifth, low-latency data pipelines must connect surrogate sensors and periodic HRMS with predictive models for real-time deployment; fluorescence-based surrogates provide a solution yet exhibit an indirect correlation to TP toxicity [55].

Table 7. Key challenges and recommended research actions

Challenge	Why it matters	Recommended action
Scarce TP datasets	Models are trained on stable parents; transient TPs are underrepresented	Build open, FAIR-compliant repositories linking structures, MS/MS spectra, confidence levels and effect data from AOP studies
Matrix complexity	EfOM and anions change radical pools and TP distributions	Generate matrix-resolved training data; include matrix descriptors as model inputs
Mixture toxicity	TPs co-occur with parents and each other; additivity may fail	Benchmark CA/IA predictions against measured effluent responses; apply effect-directed analysis
Model uncertainty and domain	Predictions outside the training domain mislead control	Report applicability domains and uncertainty; default to precaution outside domain
Regulatory metrics	Concentration-based targets reward disappearance	Adopt effect- or risk-based performance indicators (NEI*, RQ_{mix}, bioassay trigger values)
Real-time integration	Control needs timely signals	Pilot EEM and online HRMS surrogates; validate against bioassays under the T3 tier

Limitations of this review. The review is narrative, and the compound-level evidence in Table 2 is restricted to cases for which primary data could be confirmed; many relevant studies on other contaminant classes and oxidants are therefore not tabulated. The proposed framework has not been implemented or experimentally validated, and its performance claims remain hypotheses to be tested using the roadmap in Table 6.

7. Conclusions

Parent-compound removal is a necessary but insufficient indicator of AOP performance. Field and laboratory evidence shows that oxidation can generate TPs with equal or greater toxicity than the parent, that the outcome is compound-, oxidant- and matrix-specific, and that post-treatment frequently removes a large fraction of the TPs formed. Standard targeted analysis cannot see most of this chemistry, and non-target HRMS reduces but does not eliminate the blind spot. The framework proposed here couples DFT, graph-based machine learning, in silico TP libraries, HRMS prioritization, QSAR toxicity prediction and mixture modelling to a risk-based control logic anchored by measured effect data. Its value will depend on open TP datasets, uncertainty-aware models and staged experimental validation. We recommend that AOP studies report

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residual toxicity or risk, together with identification confidence for TPs, alongside conventional removal metrics.

Declarations

Conflict of 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.

References

1. Y. Luo et al., "A review on the occurrence of micropollutants in the aquatic environment and their fate and removal during wastewater treatment," Sci. Total Environ., vol. 473–474, pp. 619–641, 2014, doi: 10.1016/j.scitotenv.2013.12.065.
2. O. M. Rodriguez-Narvaez, J. M. Peralta-Hernandez, A. Goonetilleke, and E. R. Bandala, "Treatment technologies for emerging contaminants in water: A review," Chem. Eng. J., vol. 323, pp. 361–380, 2017, doi: 10.1016/j.cej.2017.04.106.
3. W. H. Glaze, J.-W. Kang, and D. H. Chapin, "The chemistry of water treatment processes involving ozone, hydrogen peroxide and ultraviolet radiation," Ozone Sci. Eng., vol. 9, no. 4, pp. 335–352, 1987, doi: 10.1080/01919518708552148.
4. D. B. Miklos, C. Remy, M. Jekel, K. G. Linden, J. E. Drewes, and U. Hübner, "Evaluation of advanced oxidation processes for water and wastewater treatment – A critical review," Water Res., vol. 139, pp. 118–131, 2018, doi: 10.1016/j.watres.2018.03.042.
5. G. Boczkaj and A. Fernandes, "Wastewater treatment by means of advanced oxidation processes at basic pH conditions: A review," Chem. Eng. J., vol. 320, pp. 608–633, 2017, doi: 10.1016/j.cej.2017.03.084.
6. F. Ghanbari and M. Moradi, "Application of peroxymonosulfate and its activation methods for degradation of environmental organic pollutants: Review," Chem. Eng. J., vol. 310, pp. 41–62, 2017, doi: 10.1016/j.cej.2016.10.064.
7. J. Wang and S. Wang, "Reactive species in advanced oxidation processes: Formation, identification and reaction mechanism," Chem. Eng. J., vol. 401, Art. no. 126158, 2020, doi: 10.1016/j.cej.2020.126158.
8. G. V. Buxton, C. L. Greenstock, W. P. Helman, and A. B. Ross, "Critical review of rate constants for reactions of hydrated electrons, hydrogen atoms and hydroxyl radicals (•OH/•O−) in aqueous solution," J. Phys. Chem. Ref. Data, vol. 17, no. 2, pp. 513–886, 1988, doi: 10.1063/1.555805.
9. P. Neta, R. E. Huie, and A. B. Ross, "Rate constants for reactions of inorganic radicals in aqueous solution," J. Phys. Chem. Ref. Data, vol. 17, no. 3, pp. 1027–1284, 1988, doi: 10.1063/1.555808.
10. C. von Sonntag and U. von Gunten, Chemistry of ozone in water and wastewater treatment: From basic principles to applications, London, U.K.: IWA Publishing, 2012, doi: 10.2166/9781780400839.
11. J. Lee, U. von Gunten, and J.-H. Kim, "Persulfate-based advanced oxidation: Critical assessment of opportunities and roadblocks," Environ. Sci. Technol., vol. 54, no. 6, pp. 3064–3081, 2020, doi: 10.1021/acs.est.9b07082.
12. D. A. Armstrong et al., "Standard electrode potentials involving radicals in aqueous solution: Inorganic radicals (IUPAC Technical Report)," Pure Appl. Chem., vol. 87, no. 11–12, pp. 1139–1150, 2015, doi: 10.1515/pac-2014-0502.
13. Y. Yang, J. J. Pignatello, J. Ma, and W. A. Mitch, "Comparison of halide impacts on the efficiency of contaminant degradation by sulfate and hydroxyl radical-based advanced oxidation processes (AOPs)," Environ. Sci. Technol., vol. 48, no. 4, pp. 2344–2351, 2014, doi: 10.1021/es404118q.
14. M. J. Bentel et al., "Defluorination of per- and polyfluoroalkyl substances (PFASs) with hydrated electrons: Structural dependence and implications to PFAS remediation and management," Environ. Sci. Technol., vol. 53, no. 7, pp. 3718–3728, 2019, doi: 10.1021/acs.est.8b06648.
15. J. R. Bolton, K. G. Bircher, W. Tumas, and C. A. Tolman, "Figures-of-merit for the technical development and application of advanced oxidation technologies for both electric- and solar-driven systems (IUPAC Technical Report)," Pure Appl. Chem., vol. 73, no. 4, pp. 627–637, 2001, doi: 10.1351/pac200173040627.
16. D. Fatta-Kassinos, M. I. Vasquez, and K. Kümmerer, "Transformation products of pharmaceuticals in surface waters and wastewater formed during photolysis and advanced oxidation processes – Degradation, elucidation of byproducts and assessment of their biological potency," Chemosphere, vol. 85, no. 5, pp. 693–709, 2011, doi: 10.1016/j.chemosphere.2011.06.082.
17. J. Völker, M. Stapf, U. Miehe, and M. Wagner, "Systematic review of toxicity removal by advanced wastewater treatment technologies via ozonation and activated carbon," Environ. Sci. Technol., vol. 53, no. 13, pp. 7215–7233, 2019, doi: 10.1021/acs.est.9b00570.
18. C. Prasse, D. Stalter, U. Schulte-Oehlmann, J. Oehlmann, and T. A. Ternes, "Spoilt for choice: A critical review on the chemical and biological assessment of current wastewater treatment technologies," Water Res., vol. 87, pp. 237–270, 2015, doi: 10.1016/j.watres.2015.09.023.
19. A. Magdeburg, D. Stalter, M. Schlüsener, T. Ternes, and J. Oehlmann, "Evaluating the efficiency of advanced wastewater treatment: Target analysis of organic contaminants and (geno-)toxicity assessment tell a different story," Water Res., vol. 50, pp. 35–47, 2014, doi: 10.1016/j.watres.2013.11.041.
20. C. J. E. Davey, A. Dubey, P. Keutmann, T. L. ter Laak, L. de Senerpont Domis, and A. P. van Wezel, "Wastewater remediation of pharmaceuticals with ozone and granular active carbon: A risk-driven approach," Environ. Sci.: Water Res. Technol., vol. 11, pp. 2986–3000, 2025, doi: 10.1039/D5EW00600G.
21. T. Schulze et al., "Identification of a phytotoxic photo-transformation product of diclofenac using effect-directed analysis," Environ. Pollut., vol. 158, no. 5, pp. 1461–1466, 2010, doi: 10.1016/j.envpol.2009.12.032.
22. E. Cruz Muñoz, G. Tseberlidis, A. H. Husien, S. Binetti, and F. Gosetti, "Identification and ecotoxicity of the diclofenac transformation products formed by photolytic and photocatalytic processes," Environ. Sci. Pollut. Res., vol. 32, no. 21, pp. 12700–12712, 2025, doi: 10.1007/s11356-025-36466-5.
23. M. M. Gómez-Ramos et al., "Chemical and toxicological evolution of the antibiotic sulfamethoxazole under ozone treatment in water solution," J. Hazard. Mater., vol. 192, no. 1, pp. 18–25, 2011, doi: 10.1016/j.jhazmat.2011.04.072.

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24. A. Agüera, L. A. Pérez Estrada, I. Ferrer, E. M. Thurman, S. Malato, and A. R. Fernández-Alba, "Application of time-of-flight mass spectrometry to the analysis of phototransformation products of diclofenac in water under natural sunlight," J. Mass Spectrom., vol. 40, no. 7, pp. 908–915, 2005, doi: 10.1002/jms.867.
25. J. E. Schollée, M. Bourgin, U. von Gunten, C. S. McArdell, and J. Hollender, "Non-target screening to trace ozonation transformation products in a wastewater treatment train including different post-treatments," Water Res., vol. 142, pp. 267–278, 2018, doi: 10.1016/j.watres.2018.05.045.
26. R. Gulde, M. Rutsch, B. Clerc, J. E. Schollée, U. von Gunten, and C. S. McArdell, "Formation of transformation products during ozonation of secondary wastewater effluent and their fate in post-treatment: From laboratory- to full-scale," Water Res., vol. 200, Art. no. 117200, 2021, doi: 10.1016/j.watres.2021.117200.
27. M. Bourgin et al., "Evaluation of a full-scale wastewater treatment plant upgraded with ozonation and biological post-treatments: Abatement of micropollutants, formation of transformation products and oxidation by-products," Water Res., vol. 129, pp. 486–498, 2018, doi: 10.1016/j.watres.2017.10.036.
28. U. von Gunten, "Ozonation of drinking water: Part I. Oxidation kinetics and product formation," Water Res., vol. 37, no. 7, pp. 1443–1467, 2003, doi: 10.1016/S0043-1354(02)00457-8.
29. M. Trojanowicz, A. Bojanowska-Czajka, I. Bartosiewicz, and K. Kulisa, "Advanced oxidation/reduction processes treatment for aqueous perfluorooctanoate (PFOA) and perfluorooctanesulfonate (PFOS) – A review of recent advances," Chem. Eng. J., vol. 336, pp. 170–199, 2018, doi: 10.1016/j.cej.2017.10.153.
30. J. L. Bolton, M. A. Trush, T. M. Penning, G. Dryhurst, and T. J. Monks, "Role of quinones in toxicology," Chem. Res. Toxicol., vol. 13, no. 3, pp. 135–160, 2000, doi: 10.1021/tx9902082.
31. R. M. LoPachin, T. Gavin, A. DeCaprio, and D. S. Barber, "Application of the hard and soft, acids and bases (HSAB) theory to toxicant–target interactions," Chem. Res. Toxicol., vol. 25, no. 2, pp. 239–251, 2012, doi: 10.1021/tx2003257.
32. G. P. Anipsitakis, D. D. Dionysiou, and M. A. Gonzalez, "Cobalt-mediated activation of peroxymonosulfate and sulfate radical attack on phenolic compounds. Implications of chloride ions," Environ. Sci. Technol., vol. 40, no. 3, pp. 1000–1007, 2006, doi: 10.1021/es050634b.
33. P. Kovacic and R. Somanathan, "Nitroaromatic compounds: Environmental toxicity, carcinogenicity, mutagenicity, therapy and mechanism," J. Appl. Toxicol., vol. 34, no. 8, pp. 810–824, 2014, doi: 10.1002/jat.2980.
34. B. I. Escher and K. Fenner, "Recent advances in environmental risk assessment of transformation products," Environ. Sci. Technol., vol. 45, no. 9, pp. 3835–3847, 2011, doi: 10.1021/es1030799.
35. M. Krauss, H. Singer, and J. Hollender, "LC–high resolution MS in environmental analysis: From target screening to the identification of unknowns," Anal. Bioanal. Chem., vol. 397, no. 3, pp. 943–951, 2010, doi: 10.1007/s00216-010-3608-9.
36. P. Gago-Ferrero, E. L. Schymanski, A. A. Bletsou, R. Aalizadeh, J. Hollender, and N. S. Thomaidis, "Extended suspect and non-target strategies to characterize emerging polar organic contaminants in raw wastewater with LC-HRMS/MS," Environ. Sci. Technol., vol. 49, no. 20, pp. 12333–12341, 2015, doi: 10.1021/acs.est.5b03454.
37. J. Hollender, E. L. Schymanski, H. P. Singer, and P. L. Ferguson, "Nontarget screening with high resolution mass spectrometry in the environment: Ready to go?" Environ. Sci. Technol., vol. 51, no. 20, pp. 11505–11512, 2017, doi: 10.1021/acs.est.7b02184.
38. E. L. Schymanski et al., "Identifying small molecules via high resolution mass spectrometry: Communicating confidence," Environ. Sci. Technol., vol. 48, no. 4, pp. 2097–2098, 2014, doi: 10.1021/es5002105.
39. I. Michael-Kordatou et al., "Dissolved effluent organic matter: Characteristics and potential implications in wastewater treatment and reuse applications," Water Res., vol. 77, pp. 213–248, 2015, doi: 10.1016/j.watres.2015.03.011.
40. A. D. Becke, "Density-functional thermochemistry. III. The role of exact exchange," J. Chem. Phys., vol. 98, no. 7, pp. 5648–5652, 1993, doi: 10.1063/1.464913.
41. C. Lee, W. Yang, and R. G. Parr, "Development of the Colle-Salvetti correlation-energy formula into a functional of the electron density," Phys. Rev. B, vol. 37, no. 2, pp. 785–789, 1988, doi: 10.1103/PhysRevB.37.785.
42. R. G. Parr and W. Yang, "Density functional approach to the frontier-electron theory of chemical reactivity," J. Amer. Chem. Soc., vol. 106, no. 14, pp. 4049–4050, 1984, doi: 10.1021/ja00327a008.
43. P. C. St. John, Y. Guan, Y. Kim, S. Kim, and R. S. Paton, "Prediction of organic homolytic bond dissociation enthalpies at near chemical accuracy with sub-second computational cost," Nat. Commun., vol. 11, Art. no. 2328, 2020, doi: 10.1038/s41467-020-16201-z.
44. K. Yang et al., "Analyzing learned molecular representations for property prediction," J. Chem. Inf. Model., vol. 59, no. 8, pp. 3370–3388, 2019, doi: 10.1021/acs.jcim.9b00237.
45. S. Zhong, J. Hu, X. Yu, and H. Zhang, "Molecular image-convolutional neural network (CNN) assisted QSAR models for predicting contaminant reactivity toward OH radicals: Transfer learning, data augmentation and model interpretation," Chem. Eng. J., vol. 408, Art. no. 127998, 2021, doi: 10.1016/j.cej.2020.127998.
46. S. Kern, K. Fenner, H. P. Singer, R. P. Schwarzenbach, and J. Hollender, "Identification of transformation products of organic contaminants in natural waters by computer-aided prediction and high-resolution mass spectrometry," Environ. Sci. Technol., vol. 43, no. 18, pp. 7039–7046, 2009, doi: 10.1021/es901979h.
47. J. Wicker et al., "enviPath – The environmental contaminant biotransformation pathway resource," Nucleic Acids Res., vol. 44, no. D1, pp. D502–D508, 2016, doi: 10.1093/nar/gkv1229.
48. Y. Djoumbou-Feunang, J. Fiamoncini, A. Gil-de-la-Fuente, R. Greiner, C. Manach, and D. S. Wishart, "BioTransformer: A comprehensive computational tool for small molecule metabolism prediction and metabolite identification," J. Cheminform., vol. 11, Art. no. 2, 2019, doi: 10.1186/s13321-018-0324-5.
49. A. Mayr, G. Klambauer, T. Unterthiner, and S. Hochreiter, "DeepTox: Toxicity prediction using deep learning," Front. Environ. Sci., vol. 3, Art. no. 80, 2016, doi: 10.3389/fenvs.2015.00080.
50. A. Tropsha, "Best practices for QSAR model development, validation, and exploitation," Mol. Inform., vol. 29, no. 6–7, pp. 476–488, 2010, doi: 10.1002/minf.201000061.
51. A. Cherkasov et al., "QSAR modeling: Where have you been? Where are you going to?" J. Med. Chem., vol. 57, no. 12, pp. 4977–5010, 2014, doi: 10.1021/jm4004285.

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52. S. Zhong et al., “Machine learning: New ideas and tools in environmental science and engineering,” Environ. Sci. Technol., vol. 55, no. 18, pp. 12741–12754, 2021, doi: 10.1021/acs.est.1c01339.
53. T. Backhaus and M. Faust, “Predictive environmental risk assessment of chemical mixtures: A conceptual framework,” Environ. Sci. Technol., vol. 46, no. 5, pp. 2564–2573, 2012, doi: 10.1021/es2034125.
54. W. Brack, “Effect-directed analysis: A promising tool for the identification of organic toxicants in complex mixtures?” Anal. Bioanal. Chem., vol. 377, no. 3, pp. 397–407, 2003, doi: 10.1007/s00216-003-2139-z.
55. K. R. Murphy, C. A. Stedmon, D. Graeber, and R. Bro, “Fluorescence spectroscopy and multi-way techniques. PARAFAC,” Anal. Methods, vol. 5, no. 23, pp. 6557–6566, 2013, doi: 10.1039/C3AY41160E.

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