



Holistic overview on disinfection by-products formation and their analytical characterization

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Abbreviations: 2D IC-CD, Two-dimensional ion chromatography with conductivity detection; 4Cl3Me, 4-chloro-3-methylphenol; BAcAm, Bromoacetamide; BCAA, Bromochloroacetic acid; BCACAm, Bromochloroacetamide; BCAN, Bromochloroacetonitrile; BCNM, Bromochloronitromethane; BDCAA, Bromodichloroacetic acid; BDCACAm, Bromodichloroacetamide; BDCM, Bromodichloromethane; BDCNM, Bromodichloronitromethane; BIAA, Bromoiodoacetic acid; BIACAm, Bromoiodoacetamide; BNM, Bromonitromethane; BP, Bromophenol; BSTFA, Bistrimethylsilyltrifluoroacetamide; CA, Chloroacetone; CACAm, Chloroacetamide; CAR, Carboxen; CD, Conductivity detection; CDBAA, Chlorodibromoacetic acid; CIAA, Chloroiodoacetic acid; CIACAm, Chloroiodoacetamide; CNM, Chloronitromethane; CP, Chlorophenol; CWR, Carbon wide range; DAD, Diode-array detector; DAS, Differential absorbance spectroscopy; DBA, Dibromoacetone; DBAA, Dibromoacetic acid; DBACAm, Dibromoacetamide; DBAN, Dibromoacetonitrile; DBCAA, Dibromochloroacetic acid; DBCACAm, Dibromochloroacetamide; DBCM, Dibromochloromethane; DBCNM, Dibromochloronitromethane; DBNM, Dibromonitromethane; DBPh, Dibromophenol; DBPs, Disinfection by-products; DCA, Dichloroacetone; DCAA, Dichloroacetic acid; DCACAm, Dichloroacetamide; DCAN, Dichloroacetonitrile; DCM, Dichloromethane; DCNM, Dichloronitromethane; DCP, Dichlorophenol; DIAA, Diiodoacetic acid; DIACAm, Diiodoacetamide; DLLME, Dispersive liquid-liquid extraction; DMP, Dimethylphenol; DOC, Dissolved organic carbon; DOM, Dissolved organic matter; DSDME, Directly suspended droplet microextraction; DVB, Divinylbenzene; DWD, Drinking water directive; ECD, Electron capture detection; EEM, Excitation-emission matrix; ESI, Electrospray ionization; EU, European Union; FA, Fulvic acid; FEEM, Fluorescence excitation-emission matrix; FRI, Fluorescence regional integration; FT-ICR-MS, Fourier Transform Ion Cyclotron Resonance Mass Spectrometry; GC, Gas chromatography; HA, Humic acid; HAAs, Haloacetic acids; HALS, Haloacetaldehydes; HAMS, Haloacetamides; HANs, Haloacetonitriles; HF-LPME, Hollow-fibre liquid phase microextraction; HILIC, Hydrophilic interaction liquid chromatography; HiSorb, High capacity sorptive extraction; HKs, Haloketones; HLB, Hydrophilic lipophilic balanced; HNM, Halonitromethanes; HPIC, High-performance ion chromatography; HPs, Halophenols; HPSEC, High-performance size exclusion chromatography; HS, Headspace; I_{450} , Emission intensity at 450 nm; I_{500} , Emission intensity at 500 nm; IC, Ion chromatography; ICP, Inductively coupled plasma; LC, Liquid chromatography; LLE, Liquid-liquid extraction; LMW, Low molecular weight; LOD, Limit of detection; LOQ, Limit of quantification; MBAA, Monobromoacetic acid; MBAN, Monobromoacetonitrile; MCAA, Monochloroacetic acid; MCAN, Monochloroacetonitrile; MEPS-PTV, Microextraction by packed sorbent with programmed temperature vaporizer; MIAA, Monoiodoacetic acid; MLLE, Micro liquid-liquid extraction; MRM, Multiple reaction monitoring; MS, Mass spectrometry; MTBE, Methyl-tert-butyl ether; *n.d.*, value not defined; N-DBPs, Nitrogenous disinfection by-products; NDMA, N-Nitrosodimethylamine; NMR, Nuclear magnetic resonance; NOM, Natural organic matter; OCD, Organic carbon detector; OCs, Anthropogenic organic chemicals; P&T, Purge and trap; PARAFAC, Parallel factor analysis method; PBP, Pentabromophenol; PCP, Pentachlorophenol; PDMS, Polydimethylsiloxane; POM, Particulate organic matter; PP, Picking method; REFIT, Regulatory fitness and performance programme; RPLC, Reversed-phase liquid chromatography; SBSE, Stir bar sorptive extraction; SEC, Size exclusion chromatography; SFC, Supercritical fluid chromatography; SPE, Solid-phase extraction; SPME, Solid-phase microextraction; SUVA₂₅₄, Specific value of absorbance of ultraviolet light at 254 nm; TBAA, Tribromoacetic acid; TBACAm, Tribromoacetamide; TBM, Bromoform; TBNM, Tribromonitromethane; TBP, Tribromophenol; TCA, Trichloroacetone; TCAA, Trichloroacetic acid; TCACAm, Trichloroacetamide; TCAN, Trichloroacetonitrile; TCM, Chloroform; TCNM, Trichloronitromethane; TD-GC-MS, Thermal desorption GC-MS; TeBA, Tetrabromoacetone; TeBP, Tetrabromophenol; TeCA, Tetrachloroacetone; TeCP, Tetrachlorophenol; TF-SPME, Thin-film SPME; THMFP, Trihalomethane formation potential; THMs, Trihalomethanes; TOC, Total organic carbon; TOX, Total organic halogen; US EPA, United States Environmental Protection Agency; UV, Ultraviolet; UVA₂₅₄, Absorbance of ultraviolet light at 254 nm; WHO, World Health Organization; WTP, Water treatment plant; WWTP, Wastewater treatment plant; ZP4WC, ZeroPollution4Water Cluster; λ_{em} , Emission wavelength; λ_{ex} , Excitation wavelength.

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ABSTRACT

Water disinfection by-products (DBPs) encompass a diverse array of chemical compounds with relevant toxicity that result from the interaction between disinfectants and the organic or inorganic substances present in natural waters. This review provides a comprehensive insight into DBP formation and their analytical quantification, addressing a critical topic in water treatment and public health. DBPs are attracting increasing attention of the research community and water-related companies due to current revisions in regulations, and the recognized need for environmental/health/governmental institutions to gather more data on these contaminants in drinking water. However, the knowledge on the formation and control of certain contaminants and the analytical techniques not always promptly advance in response to the requirements of regulation. For instance, in the case of DBPs, the analytical protocols for their quantification are not well developed for many families/compounds and vary significantly due to DBPs chemistry and low stability. Therefore, there remains a significant gap in the literature regarding the critical analysis of the advances of research and confirmed analytical procedures on this topic. This review gives an in-depth and holistic analysis on: i) DBPs precursor compounds in source waters, such as natural organic matter (NOM) and anthropogenic organic chemicals (OCs); ii) chemical composition, reactivity and quantification methods for these precursors; iii) mechanisms of DBP formation during disinfection; iv) advances in analytical detection and quantification for DBPs; and vi) current regulatory framework. It further highlights emerging challenges, offering insights into evolving regulatory, technological, and scientific landscapes.

1. Introduction

Over the past decade, the increase in globalization, industrialization and agricultural activities have taken a toll on several resources, such as water, soil and air. Water contamination, and specifically drinking water contamination, has been at the forefront of recent debates worldwide, as the presence of organic matter and pathogens, including viruses, protozoa and bacteria, in surface and drinking water leads to the imperative need for treatments capable of eliminating them [123]. These treatments usually involve several process steps, such as coagulation and flocculation, sedimentation, filtration and disinfection. However, the efficiency of the treatment train is highly affected due to the increasing loads on natural organic matter and organic pollutants found in the raw water [88]. But, whatever techniques are used, the need to add oxidizing treatment agents is mandatory in many countries to inactivate water-borne pathogens, guaranteeing the safety of drinking water for human consumption. When disinfection is performed (e.g. using chlorine gas, hypochlorite, chloramines, chlorine dioxide, ozone), usually with free chlorine, the disinfectant interacts with natural organic matter (NOM) and leads to the formation of several unwanted by-products, the disinfection by-products (DBPs) [143]. The majority of DBPs found in drinking water include trihalomethanes (THMs), haloacetic acids (HAAs), haloacetamides (HANs) and haloketones (HKs) in concentrations ranging from ng L^{-1} to $\mu\text{g L}^{-1}$ [49,205,242]. Given the increasing complexity of NOM and organic pollutants that end up in the water, emerging DBPs can be found. These are a particular concern as they may be more complex and toxic [117]. To overcome the incidence of DBPs in water, several regulatory agencies have defined recommended or enforceable limits for some DBPs, focused on DBPs that are better known (e.g., THMs and HAAs) and not the emerging DBPs (Gilca, 2020). However, two main factors must be considered regarding DBPs: (i) the possibility of detecting them at very low concentrations, (ii) the recognition of the toxicological effects and the definition of a proper toxicological threshold.

The concentrations at which the DBPs are present in drinking water pose a challenge in the choice of the analytical techniques to assess them, as the limits of detection and quantification and selectivity of

some equipment may prevent their use [239]. Additionally, real-time monitoring techniques that allow the quantification of these DBPs throughout the entire water distribution network are an urgent need [193]. The behaviour of DBPs can pose an additional difficulty as they may present challenges during analysis that must be considered, such as toxicity, volatility and acidic character. Therefore, several quantification techniques have been optimized over the years and modified to include more DBPs classes [239]. Considering this complex water context, this review contributes to the understanding of anthropogenic impacts on water quality and the efficacy of disinfection processes, which cannot be dissociated from the formation of DBPs. Therefore, it highlights the interplay between water chemistry, DBPs formation, regulatory measures, and emerging analytical techniques, establishing correlations between these vectors. This holistic vision supports the decision-making on the best management/control strategies to ensure safe drinking water distribution.

1.1. DBP classification

Understanding the classification of DBPs is essential for assessing their potential risks to human health and the environment, as well as for developing effective prevention and mitigation strategies in water treatment practices. These strategies may encompass the abatement of DBPs precursors before the disinfection step or the removal of the DBPs from disinfected water before supplying it to the consumers.

More than 700 DBPs have already been identified in drinking water. These compounds can be classified based on their chemical structure, formation pathway, and toxicity. One common classification scheme categorizes DBPs into organic and inorganic groups.

With regard to organic DBPs, these are usually categorized as aliphatic, alicyclic and aromatic. From these, the main groups that are generally considered are THMs, HAAs, HANs, HKs, haloacetamides (HAMs), haloacetaldehydes (HALs) and N-nitrosamines [146].

THMs were the first identified DBP group in disinfected water [192]. They are formed through the chlorination or chloramination of organic matter in water, which also contains natural bromide or iodide ions. THMs normally include the following compounds: chloroform,

bromodichloromethane (BDCM), dibromochloromethane (DBCM), and bromoform. While chloroform is the most abundant THM, brominated species tend to be more toxic. Long-term exposure to elevated THM levels has been associated with adverse health effects, including cancer and reproductive issues [16].

HAA are another significant group of DBPs, which include monochloroacetic acid (MCAA), dichloroacetic acid (DCAA), trichloroacetic acid (TCAA), monobromoacetic acid (MBAA), and dibromoacetic acid (DBAA). Like THMs, HAAs have been linked to adverse health outcomes, including cancer and developmental abnormalities. Current regulations and guidelines for disinfected water include limits regarding both THMs and HAAs [219,224,242].

The use of alternative disinfectants by changing from free chlorine to monochloramine, as well as the reactions between the disinfectant and nitrogenated organics, may lead to the formation of nitrogen-containing DBPs such as HANs and HAMs [229]. These unregulated DBPs are considered to be more cyto- and genotoxic than THMs and HAAs, as can be seen in the study performed by Lau et al. [122]. To further understand these unregulated DBPs, Hebert et al. [92] have performed a ranking method to prioritize unregulated DBPs, regarding their health effects, occurrence and toxicity, showing that depending on the type of DBP these parameters may vary [92]. On the other hand, a global statistical assessment of the effect of water quality parameters on the formation and regulatory exceedances of major DBPs in finished drinking waters, across diverse geographic regions in the world, was performed by Costa et al. [40]. Additionally, it is recognized that the comprehension of the toxicology effects of DBP mixtures remains limited [40,252].

It is understood by the scientific community that even if these unregulated groups of DBPs may contribute more to the overall toxicity, they do not account for all adverse effects in human health [47]. Literature indicates that the identified DBPs may contribute to only up to 40% of the total organic halogen (TOX) in drinking water, indicating that most halogenated DBPs in drinking water remain undiscovered. Furthermore, the novel disinfection strategies involving alternative

disinfectants will lead to unknown emerging DBPs [262]. Gilca et al. [82] mentioned that emerging DBPs include chlorate, N-nitrosamines, aldehydes, unregulated THMs (e.g., dibromomethane), unregulated HAAs (e.g., bromochloroacetic acid), halopyroles, haloanisoles, chlorophenols, HANs, HKs, halonitromethanes, iodoTHMs, among others. Fig. 1 shows a possible classification of organic DBPs based on their chemical structure, emphasizing the ones that are emergent.

Inorganic DBPs are also an important group that should be considered when assessing drinking water quality. These compounds result from the reaction between the disinfectant and inorganic compounds present in water or present as impurities of the disinfectant itself. Chlorite and chlorate are produced from the decomposition of sodium hypochlorite when stored or when chlorine dioxide, another commonly used disinfectant, reacts with water. Chlorite and chlorate are regulated due to their potential adverse health effects, including methemoglobinemia (blue baby syndrome) and thyroid dysfunction [242]. Additionally, the presence of bromide ions in water sources can lead to the formation of bromate, an inorganic DBP that is regulated (strict drinking water standard of $10 \mu\text{g L}^{-1}$) due to its carcinogenicity. Bromate forms when bromide ions react with ozone or hypochlorite in water disinfection processes [155].

2. DBP Precursor Compounds in Source Waters

2.1. Types and origin of Natural Organic Matter (NOM) and anthropogenic organic chemicals (OCs) in source water

2.1.1. Chemical-structural diversity of organic matter

NOM constitutes a complex, polydisperse mixture of organic compounds derived from the biogeochemical degradation and humification of vegetal and faunal residues. It includes humic substances (humic acids, fulvic acids, and humin), as well as non-humic substances such as proteins, carbohydrates, lipids, and organic acids [158]. In aqueous systems, NOM serves as the primary precursor for the formation of DBPs.

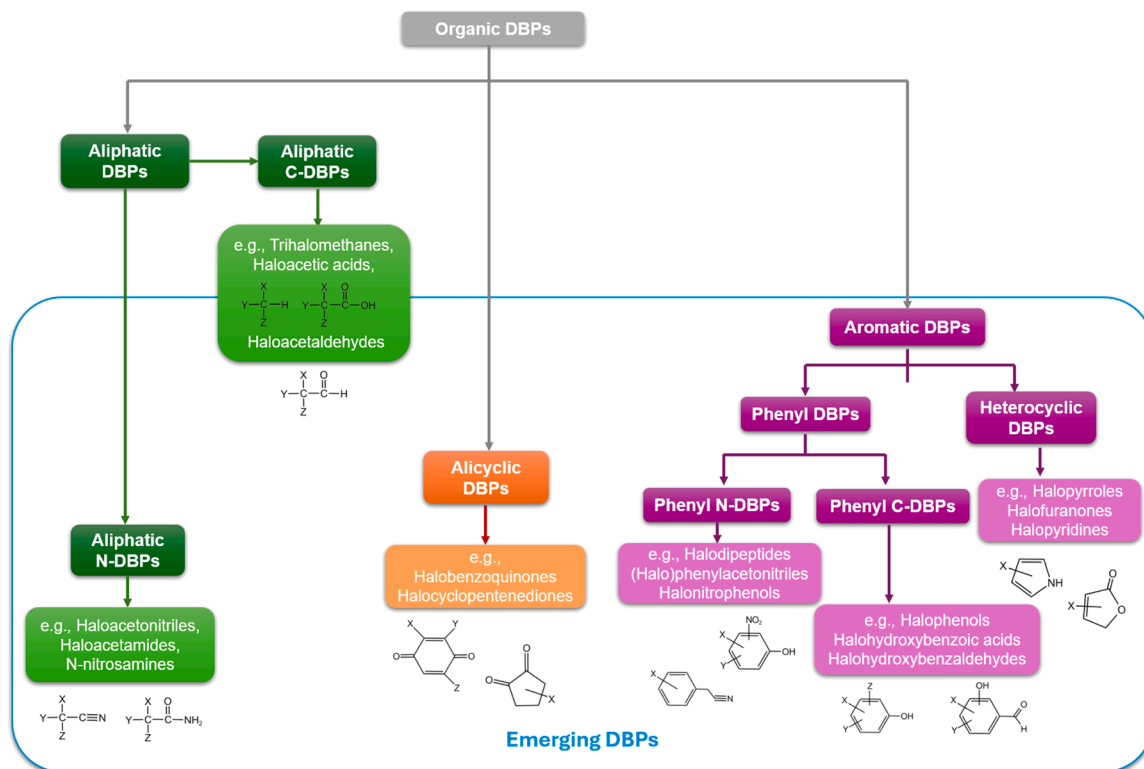


Fig. 1. Possible classification of organic DBPs, showing which DBP classes are emergent. For aliphatic C-DBPs, haloacetaldehydes are considered emergent, along with some THMs and HAAs. X, Y and Z represent Cl, Br, I, H.

While NOM partitions into dissolved (DOM) and particulate (POM) fractions, DOM is the predominant driver of DBP synthesis; this is due to the fact that POM is largely sequestered and removed during the coagulation and filtration stages of the treatment train [84]. Therefore, it is important to measure and characterize its concentration, composition, and reactivity to predict DBP formation and optimize treatment processes.

DOM plays a pivotal role in biogeochemical cycles and can be classified into distinct fractions based on their size and solubility properties [50,125]. DOM is operationally defined as the fraction of organic matter capable of permeating a 0.45 μm membrane, encompassing molecular species ranging from discrete solutes to colloidal aggregates. Although colloidal characteristics influence physicochemical transport behaviour and stability, the formation potential of DBPs is governed primarily by the chemical functionalities and intrinsic reactivity of the DOM matrix.

DOM embodies a complex mixture of organic compounds characterized by diverse molecular sizes, physical attributes, and chemical properties. Within DOM, a diverse array of functional groups exists, including aromatic, aliphatic, phenolic, and quinone structures, contributing to its heterogeneity [65,91,90]. Further classification of DOM into hydrophobic, transphilic, and hydrophilic categories based on water affinity also offers valuable insights [125]. Each DOM constituent can be further delineated based on sorption properties into acids, neutrals, and bases. The hydrophobic fraction predominantly comprises humic substances, hydrocarbons, tannins, and aromatic amines, while the hydrophilic region is enriched with carboxylic acids, carbohydrates, and proteins. Transphilic components exhibit intermediate polarity, with studies indicating polysaccharides and proteins as prominent constituents [129].

Humic substances constitute a significant portion of DOM in aquatic environments, ranging from 40% to 80% [147]. Widely studied for their applications in various industries, humic substances encompass a mixture of organic compounds, including humic acid (HA), fulvic acid (FA), tannins, lignin, and fatty acids [68,275]. These substances are ubiquitous in soils, sediments, and natural aqueous matrices. Fractionation techniques such as the XAD resin method leverage differences in solubility among humic substances fractions, namely FA, HA, and humin (Fig. 2), which remain soluble, insoluble at low pH, and insoluble even under alkaline conditions, respectively [268]. Although XAD resin fractionation is extensively used to characterize NOM, the technique may affect the original molecular structure and result in varying recovery efficiency among NOM fractions. Further differentiation among these fractions is achievable through properties such as molecular weight, functional group composition, and carbon content. Generally, humin fractions exhibit higher molecular weights, increased polymerization degrees, and darker colorations [208]. While representing each constituent through a single chemical structure remains challenging, HA, FA, and humin can be depicted through representative molecular structures. Non-humic components within DOM, including proteins, polysaccharides, and aromatic amines, contribute to the intricate composition of DOM and its environmental implications [268].

Various OCs, including pharmaceuticals and personal care products, industrial chemicals and their derivatives, fungicides, pesticides, and

surfactants, possess the capacity to infiltrate drinking water sources via discharge from wastewater treatment plants or agricultural runoff. Other stemmed organic contaminants from human activities, such as unburned fossil fuels, combustion by-products (e.g., polycyclic aromatic hydrocarbons) are also common in water due to urban run-off. It should be noted that a significant number of industries produce wastewaters with high levels of organic matter; among them, we can refer to the paper and pulp industry, poultry processing, and dairy industries [3].

2.1.2. Origin-molecular structure-reactivity interrelations of organic matter

The molecular composition of DOM is intricately shaped by its origin, thereby influencing its susceptibility to both microbial and abiotic transformations [91]. Freshwater DOM typically exhibits a rich abundance of lignin-derived polyphenols sourced from vascular plant debris, contributing to the characteristic brown hue observed in rivers, lakes, and wetlands. In contrast, marine DOM commonly lacks these compounds. Nonetheless, amidst these source-specific molecular attributes, a conserved component within DOM persists across diverse aquatic systems [267]. Advanced analyses via Fourier-Transform Ion Cyclotron Resonance Mass Spectrometry (FT-ICR-MS) and Nuclear Magnetic Resonance (NMR) have identified this universal signature, characterized by carboxylic-rich alicyclic moieties (CRAM) and linear terpenoid derivatives, across diverse environments ranging from the deep ocean to microbial cultures [196]. It is postulated that prolonged degradation processes, such as photodegradation and microbial-mediated transformations, contribute to the formation of these shared structural features across diverse DOM sources [134].

Despite the recognition of common structural motifs, DOM showcases considerable molecular diversity owing to the existence of multiple isomers for each molecular formula and the flexibility in arranging structural features, as evidenced by NMR analyses. The inherent diversity and heterogeneity render DOM challenging to characterize at the molecular level, hindering a comprehensive mechanistic understanding of organic matter cycling in freshwater and marine ecosystems [158]. This intricate complexity assumes a pivotal role in the persistence and long-term preservation of organic matter in the environment [202]. Moreover, this diversity complicates prediction of DBP formation and highlights the value of high-resolution analytical techniques such as FT-ICR-MS. Therefore, addressing these knowledge gaps is imperative for advancing our comprehension of the biogeochemical processes governing organic matter dynamics in aquatic environments.

The reactivity and propensity of organic matter to act as a precursor for DBP formation are significantly influenced by its inherent characteristics, including molecular weight, aromaticity, and polarity, tied to its origin [130]. DOM originating from biological decomposition processes comprises a complex array of heterogeneous biomolecules, as already referred (Section 2.1.1), and their intricate structures and degraded states often exhibit low reactivity [253].

Both endogenous DOM originating from soil organic matter, and exogenous DOM from external sources can impact the rate of DBP formation. Humic substances are primary precursors of THMs and HAAs, while amino acids are fundamental precursors for nitrogenous disinfection by-products (N-DBPs), like HANs, HAMs, and halonitromethanes

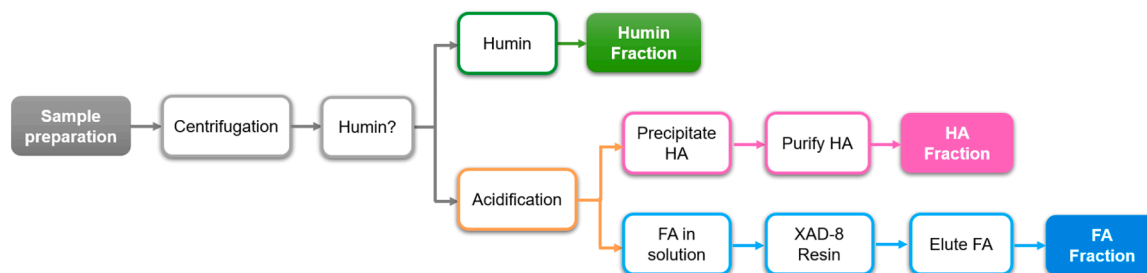


Fig. 2. The fractionation of humic substances using the XAD resin method.

(HNMs) [201]. Chlorination of amino acids may yield aldehydes, which can further transform into chloral hydrate via subsequent chlorine substitution [95]. On the other hand, algal organic matter, produced during algal eutrophication, is rich in nitrogen and features minimal aromatic structure, thus exhibiting significant potential for N-DBP production [124]. If exposed to chloramination processes, iodinated THMs may be also formed, in addition to their possible formation by the chlorination process [130].

OCs feature simpler and more defined structures than NOM/DOM, thus their relatively straightforward architecture and presence of functional groups generally lead to higher reactivity, influencing its bioavailability and potential environmental impact [265]. The OC contaminants also undergo transformations into DBPs during the disinfection processes at water treatment plants (WTPs).

While research emphasizes N-nitrosamines and iodinated DBPs due to their known carcinogenicity and toxicity, pristine water sources with minimal wastewater influence exhibit negligible levels of N-nitrosamines and their precursors, highlighting that the conventional effluents of Wastewater Treatment Plants (WWTPs) are a significant source of these DBPs [253]. Therefore, the water capture of WTPs should be placed well upstream the discharge of WWTPs. Comprehensive characterization and quantification of these multifaceted NOM fractions are imperative for modelling DBP formation potential and refining engineered treatment processes. The subsequent section evaluates prevalent analytical methodologies employed for this purpose.

2.2. Quantification methods for NOM and OCs

2.2.1. Quantification methods for NOM

The most common methods used to measure and characterize NOM in drinking water include total organic carbon (TOC), dissolved organic carbon (DOC), ultraviolet (UV) and fluorescence spectroscopies, size exclusion chromatography (SEC) and mass spectrometry (MS) approaches. Some review articles have been published on NOM quantification, for example Pan et al. [164], which mention the preparation and pretreatment methods for NOM, including isolation and concentration methods, fractionation methods and methods of analysis for general parameters used to characterize NOM (e.g., DOC, fluorescence) [164].

TOC is a widely used method to quantify the amount of organic matter in drinking water. DOC is a subset of TOC, which specifically measures the dissolved organic carbon in water, thus it is measured by filtering the sample before measuring [215]. TOC measurements provide a broad overview of the total amount of organic matter present, while DOC measurements can help to identify the effectiveness of treatment processes in removing dissolved organic compounds.

Absorbance of ultraviolet light at 254 nm (UVA_{254}) and the specific ultraviolet absorbance ($SUVA_{254}$), which is the ratio between UVA_{254} and DOC, are the most widely used surrogate parameters to quantify and characterize NOM [10,110]. In particular, $SUVA_{254}$ has been widely used because it allows the comparison of different water sources in terms of reactivity for DBP formation, usually measured as trihalomethane formation potential (THMFP) or uniform formation condition protocol [10,214]. Furthermore, the absorbance at 280 nm was also introduced because π - π^* electron transitions occur in this UV region (ca. 270–280 nm) for phenolic substances, aniline derivatives, benzoic acids, polyenes and polycyclic aromatic hydrocarbons with two or more rings [221]. Strong relationships between the molar absorbance of organic carbon at 280 nm and, on the other hand, the aromaticity of NOM and its apparent number- and weight-averaged molecular weight have been found [36,169,170,171]. UV absorbance at both 254 and 272 nm were well correlated with aromaticity, which is the percentage of the total carbon contained in aromatic subgroups [36,170,221,249]. Overall, UVA_{254} , UVA_{272} and UVA_{280} absorbances are more sensitive surrogate parameters for predicting NOM reactivity in DBP formation than DOC, as they reflect aromatic and chromophoric NOM characteristics. However, these parameters should be considered surrogate indicators rather

than universal predictors, since different NOM structures undergo multiple transformation pathways during chlorination [102]. Finally, differential absorbance at wavelengths near 272 nm ($\approx A_{272}$), corresponding to the peak of differential absorbance, was also used because it showed a strong correlation with DBPs, similar to $SUVA_{254}$ [189]. This method quantifies changes in the UV-visible absorbance of DOM caused by reactions of its chromophores with chlorine or chloramine. Different wavelengths have been used to apply the differential absorbance spectroscopy (DAS) approach. ΔUVA_{254} , ΔUVA_{272} and ΔUVA_{280} absorbances are the most used parameters to predict/monitor DBPs in chlor(am)inated waters. Furthermore, the differential absorbance at 350 nm and its logarithm were also demonstrated to be useful. As a result of its precision and sensitivity, DAS serves as a powerful tool for characterizing the formation of DBPs generated during chlorination or chloramination of natural water. However, the use of DAS to estimate DBPs has been found seasonally specific [17].

Fluorescence spectroscopy generates an emission spectrum by scanning the emission wavelength (λ_{em}), while the sample is irradiated at a single excitation wavelength (λ_{ex}). This 2D fluorescence, in contrast to UV absorbance, allows the detection of a wide range of fluorophores, but the output is restricted to a linear scan, in which the choice of excitation wavelength determines the molecules that may be identified [99]. The 2D spectra allow the determination of some indexes calculated as the ratio between the fluorescence intensity obtained at different emission wavelengths. For example, a fluorescence index, which is the ratio of the emission intensity at 450 nm to 500 nm (I_{450}/I_{500}), obtained with an excitation at 370 nm, was developed to distinguish the sources of aquatic humic acids (microbially and terrestrially derived) and was correlated with the aromaticity of fulvic acids and the potential formation of DBPs [104,145]. Other fluorescence indexes have been developed to track the formation of DBPs. A notable correlation was found between DBP formation and shifts in the emission wavelength corresponding to 50% of the maximum fluorescence intensity recorded at 320 nm excitation [64]. Furthermore, Roccaro et al. [190] have found that the differential value of the index I_{500}/I_{450} obtained at 320 nm excitation is strongly correlated with the concentration of DBPs at varying chlorination conditions (raw and treated water, chlorine dose, reaction time, and temperature) [190].

Fluorescence excitation-emission matrix (FEEM) spectroscopy, also known as three-dimensional fluorescence or fluorescence fingerprinting, is one of the most prominent methods to characterize DBP precursors because of its information-rich data, visual maps and multidimensional information provided such as indication of source, behaviour, and biogeochemical cycling of DOM, responsible for DBP formation [127,157]. Compared with 2D fluorescence, the main difference with excitation-emission matrix (EEM) is that changes in the fluorescence intensity information for the excitation and emission can be obtained simultaneously. Contour fluorescence spectrograms or 3D projections are commonly used to display EEM data. Overall, the most relevant methods used for the interpretation of EEM, summarized by Hu et al. [96] and Jing et al. [104], are the peak picking (PP) method, fluorescence regional integration (FRI) and parallel factor analysis method (PARAFAC) based on mathematical deconvolution of fluorescence peaks [96,104]. Being the most basic approach for fluorescence investigation, the PP method is frequently used in EEM fluorescence analysis to identify different fluorophores' intensities present in complex samples, such as those in natural waters. The PP method evaluates the intensities of the FEEM in specific locations on the fluorescent map, as a result of differences in their chemical composition [39,167,213]. Seven fluorophore types have been identified (Fig. 3) as representative of humic-like substances (peaks A, C, M), tyrosine-like substances (peak B), tryptophan-like substances (peak T), soil fulvic-acid (peak D), and plankton-derived substances (peak N) [133,251]. On the other hand, Chen et al. [34] employed the FRI method for quantifying spectra for DOM in which the normalized fluorescence volume was used. In this important research, EEM was subdivided into different zones to

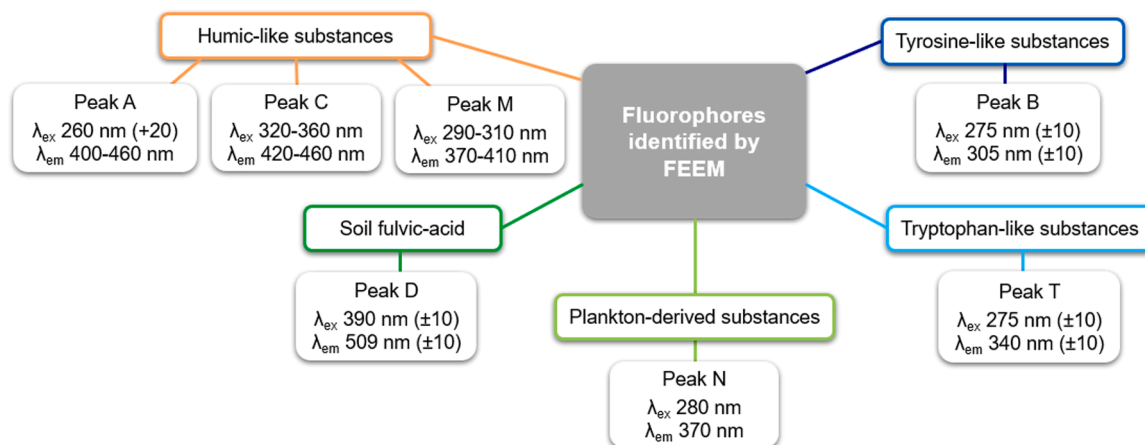


Fig. 3. – Fluorophore classification using FEEM technique [251,119,254]. λ_{ex} is the excitation wavelength and λ_{em} is the emission wavelength.

characterize the different types of fluorophores in DOM [34]. Finally, PARAFAC is a multivariate data analysis technique used to decompose EEM, considering the three-way array decomposed into a set of three lower-dimensional matrices, each representing the emission, excitation, and sample dimensions. The decomposition is based on the principle of parallel factors, which assumes that the fluorescence signals in the array are generated by a set of underlying factors that are common to all samples [211]. Researchers have found that the PARAFAC method is very useful, since it provides a more accurate estimate of the signal sources and respective contributions [127]; thus, for monitoring DBPs during water treatments and in drinking water distribution networks, it provides a stronger linear correlation between fluorophores of organic matter and DBP formation [69,76].

High-performance size exclusion chromatography (HPSEC) has been used to obtain the molecular weight distributions of natural organic matter. These separation techniques can be coupled with spectrometric detectors, which are limited to detect chromophores, leaving behind other non-absorbing NOM constituents, such as biopolymers. Korshin et al. [114] introduced the absorbance slope signal to explore the relationship between organic matter fractions and THM yields [114]. Awad et al. [13] developed models to understand how DOM, characterized by DOC, UV-Vis, and FEEM relates to HPSEC-UV and THMFP [13]. Valenti-Quiroga et al. [226] recently proposed a HPSEC-DAD-OC (HPSEC-Diode-array detector-Organic carbon detector) to predict THMs formation, with very promising results [226]. A size exclusion liquid chromatography coupled with organic carbon detector (LC-OC) and further UV₂₅₄ and organic nitrogen detectors was further developed by Huber et al. [98], offering high sensitivity, capable of detecting concentrations in the low ppb range [98]. It is used to separate and quantify DOC into six known sub-fractions based on size and chemical properties: humic substances, biopolymers, building blocks, low molecular weight (LMW) organic acids and neutrals, hydrophobic organic carbon. Building blocks are molecules of intermediate size that share chemical similarities with LMW acids and humic compounds. Therefore, this technique offers not only the possibility of advanced fingerprinting of DOC but also the ability to correlate the individual fractions with DBP classes [31,238]. Wang et al. [231] successfully established correlations between distinct DOC fractions and DBP classes [231]. Particularly, humic substances showed a strong correlation to THMFP, while the building blocks and LMW neutrals to HAAs, and the biopolymers to N-DBPs, HAMs, and HANs.

MS is a widely used method for the precise determination of the molecular composition and structure of NOM. In particular, FT-ICR-MS is a powerful technique to precisely characterise thousands of molecules in complex mixtures of NOM [218], owing to its sufficient resolution, mass accuracy and sensitivity [181]. Researchers are also increasingly

seeking other instruments, such as Orbitrap or time-of-flight (TOF) mass spectrometry [89]. These can be used with direct infusion or hyphenated to a chromatographic method for automation. Additionally, a matrix-assisted laser desorption/ionization (MALDI) technique can also be used in mass spectrometry, commonly paired with the TOF mass analyser [220]. Previous studies have also established a connection between the NOM fingerprints obtained through these characterization methods and the potential for DBP formation. FT-ICR-MS was applied for studying the molecular level change of NOM upon various disinfection processes, which is helpful to understand the reaction mechanisms and precursors, as well as to identify novel DBPs [83,234,273]. The state-of-the-art method for FT-ICR-MS analysis is the direct infusion of samples after solid-phase extraction (SPE), which, however, recovers only ~50% of dissolved organic carbon [101]. To overcome this limitation, liquid chromatography (LC) can be coupled to FT-ICR-MS to directly inject the whole sample (without extraction). Recently, Han et al. [87] applied nano-LC-FT-ICR-MS to analyse drinking water samples and found that more polar fractions of DOM and DBPs can be analysed by direct injection without the need of SPE pre-treatment [87]. More details on these methodologies can be found in the recent review by Aguilar-Alarcon [2]. In addition, matrix-assisted laser desorption/ionisation is used to identify aromatic and unsaturated components in NOM [29]. By combining these MS techniques, it is possible to obtain a comprehensive picture of the molecular structures and functions of NOM to predict the formation of DBPs and to evaluate the selectivity of the treatment [74,263,274]. However, the detected molecular information represents only the ionizable fraction of NOM rather than the entire NOM pool [178]. During electrospray ionization (ESI) analysis, ionization bias may occur because different compounds have different ionization efficiencies, which can lead to selective detection of certain molecular groups while other components remain less detectable [272]. In addition, molecular formula assignment can have uncertainties because one accurate mass value may correspond to multiple possible elemental compositions and the assigned formulas do not necessarily represent one specific chemical structure. The ESI(+) and ESI(-) modes also have different ionization preferences. Therefore, they provide complementary but still incomplete information about NOM composition. For example, ESI(+) can enhance the detection of nitrogen-containing and oxygen-poor compounds, while ESI(-) is more suitable for oxygen-rich and acidic compounds [277]. Moreover, molecular formulas obtained by FT-ICR-MS cannot directly describe the complete molecular structure of NOM, creating a gap between elemental composition and actual chemical structures [178].

Other possible methods to characterize DOM are Fourier transform infrared, NMR and Raman spectroscopies [35,118,148,194]. Field-flow fractionation is a family of chromatography-like separation techniques

used for particle and macromolecule sizing and separation, and it has also been used to characterize DOM [129].

The molecular composition of DOM varies depending on its source, which is directly related to its interaction with the production of DBPs. CHO compounds dominate terrestrial DOMs, particularly lignin- and tannin-like structures, indicating inputs from soil and plants, according to Orbitrap and FT-ICR-MS non-targeted analyses of natural fluids [172]. CHOS compounds are dominant in sulfur-rich, saline, or engineered systems, such as treated wastewater and mining-affected water, where CHOS compounds can surpass CHO as the dominant class in terms of ion density. In contrast, DOM pools derived from microorganisms or wastewater-affected water contain a relatively higher proportion of CHON compounds, which are protein-bound and derived from amino acids [87].

The chemistry of disinfection is influenced by these structural differences. Analysis of drinking water using high-resolution FT-ICR-MS mass spectrometry revealed a continuous array of halogenated CHO compounds, which react with various disinfectants. This suggests that dissolved organic matter rich in aromatic CHO compounds consistently produces carbonic byproducts (such as trihalomethanes and haloacetic acids) regardless of the disinfectant used. In contrast, dissolved organic matter rich in CHON compounds tends to produce nitrogenous byproducts: UV/chlorination of the natural organic matter in the Suwani River increased the proportion of CHON compounds only, and subsequent chlorination selectively consumed this array of CHON compounds while increasing the production of chlorinated byproducts. This directly links the abundance of CHON compounds to the availability of N-DBPs precursors. Amino acids and indole-containing molecules (such as tryptophan, phenylalanine, and 3-indolepropionic acid) are effective precursors to oxy-halogenated N-DBPs [32,115].

These results suggest that variations arising from the distribution of DOM formulation classes—carbohydrates from terrestrial inputs, carbon, nitrogen, and oxygen from microbial inputs/wastewater, and carbon, sulfur, and sulfur from saline or engineered sources—offer a mechanistic explanation, rather than a descriptive one, for the variations in DBPs types observed across DOM sources. However, it is important to note that targeted mechanistic studies remain relatively rare, and most of the associations between formulation classes and DBPs described rely on non-targeted formulation matching and compositional trend analysis (such as oxygen-to-carbon ratio changes in secondary disinfection products) rather than established reaction pathways [87, 115].

2.2.2. Quantification methods for OCs

The fastest and most cost-effective method for characterizing organic substances is UV-Vis spectroscopy. However, without prior separation method, this technique cannot distinguish between different compounds and is thus unsuitable for analysing mixed anthropogenic organic chemicals [116]. Similarly, fluorescence spectroscopy also faces the challenge of compound differentiation without a separation step when applied to anthropogenic matter. EEMs containing multi-dimensional information can be used to identify and characterize the organic matter in the effluent released by the secondary treatment stage of WWTPs, but these are often difficult to analyse [104,127,206,207]. Moreover, total fluorescence has been proven to be a good proxy variable for the identification of specific anthropogenic pollutants (e.g. pharmaceuticals, among other) in different treatment processes, such as adsorption on activated carbon, prior to disinfection [28].

Various mass spectrometry-based methods can be employed to fully characterize anthropogenic contaminants, tailored to their specific chemical properties. Predominantly, these methods utilize LC-MS or gas chromatography coupled with mass spectrometry (GC-MS). Recently, ion chromatography coupled with mass spectrometry (IC-MS) has gained attraction for characterizing polar and mobile compounds. Within this domain, different approaches are utilized depending on the desired level of identification. Targeted analysis employs analytical

standards to quantify the concentration of specific contaminants. In contrast, suspect or non-targeted analysis relies on databases for tentative identification of compounds, which must ultimately be compared to standards for full confirmation [204].

Therefore, today researchers possess the capability to comprehensively characterize the nature of contaminants present in water. Recommendations on this process can be found in Hollender and coworkers [93]. But, relating contaminants to DBP formation is not a straightforward task, as different chemical mechanisms are involved in the disinfection process [176]. However, in some specific situations where the DBP precursor contains specific moieties, this taking may be possible. For example, previous studies have employed characterization of contaminants as precursors to DBPs, based on the structure expected and needed to generate the specific DBP, namely N-nitrosodimethylamine (NDMA) [186,188]. FT-ICR-MS can be effectively used for the identification and quantification of OCs from various sources, including effluents derived from human activities [77], allowing a better understanding of their reactivity and the formation mechanisms of DBPs [101].

Fig. 4 presents a summary of the quantification procedures and methods for NOM and OCs.

3. Formation of DBPs during disinfection of water

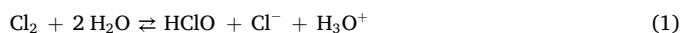
3.1. Disinfection methods – the dominant case of chlorination

Disinfection can be chemical or physical, depending on the process used. Chemical disinfectants can produce DBPs, while physical disinfection (UV light, filtration) does not, but the latter might not be efficient enough for complete disinfection, depending on the raw waters and environmental conditions [45]. In addition, physical disinfection does not produce a disinfectant residual effect, and thus cannot be used alone, where this residual effect is mandatory or preferable.

Regarding chemical disinfection, it encloses chlorine-derived disinfectants (chlorine gas, hypochlorite, chloramines, and chlorine dioxide) and ozone. Its effectiveness is related to the disinfectant used, the initial concentration, contact time, and water quality conditions such as pH and temperature [245].

Chlorine gas (Cl_2) is efficient against bacteria and viruses and is a low-cost technology [45]. The main disadvantages are security for operators and DBPs production [14]. In water with ammonia, chlorine can react with it and produce chloramines. Chloramines are disinfectants that are less effective against pathogens and generate less regulated DBPs, but can also ensure residual disinfectant effect in the distribution system [21,163]. Hypochlorite (ClO^-) is as effective against pathogens as chlorine gas, but safer for operation, although its drawback is also the formation of DBPs [14,45,80]. Chlorine dioxide (ClO_2) is more effective against bacteria than chlorine gas, hypochlorite, and chloramines. The main disadvantages of its use are the cost and the requirement for *in situ* production due to its instability during transport and storage [165,212]. Finally, ozone is the most effective chemical disinfectant against several microorganisms, including protozoa, but the most expensive for the initial capital costs [165,212]. Due to its high reactivity and instability, it is the only chemical disinfectant that cannot generate a residual effect [45]. Moreover, it should be produced *in situ* from oxygen, due to its instability.

For water disinfection purposes, free chlorine is the most widely used disinfectant due to its high oxidizing power and, thus, disinfection effectiveness, although with low selectivity. When chlorine is dissolved in water, it undergoes hydrolysis according to Eq. (1):



In turn, hypochlorous acid ionizes to form hypochlorite ion,



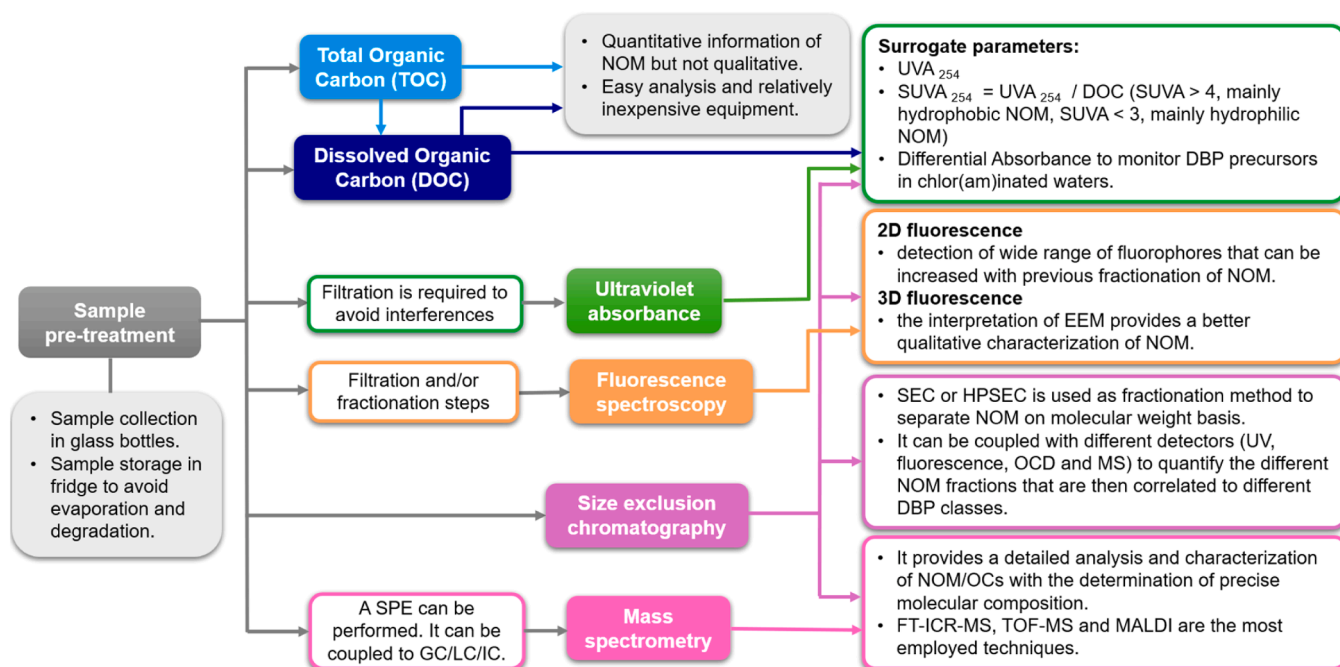
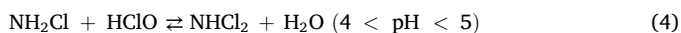
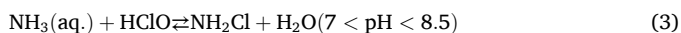


Fig. 4. – Flowchart of the quantification processes for NOM and OCs.

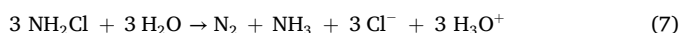
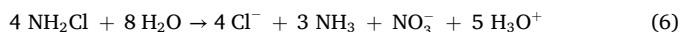
The oxidative power of the hypochlorous acid is 10% higher than that of Cl_2 , and being a weak acid ($\text{p}K_a=7.5$), indicates that at a natural water pH (6–8) both species (HClO and ClO^-) can co-exist – the above-mentioned free chlorine [153].

One way to mitigate the amount and concentration of DBPs produced by the application of chlorine is through the use of chloramines, although these are weaker disinfectants, being less effective against, e. g., viruses or protozoa [12,276]. But chloramines can also appear in water containing ammonia when using hypochlorite as the disinfectant. These can be formed by the reaction of hypochlorous acid with ammonia present in water, according to the following reactions [111]:



The evolution of the concentration of these species in water can be described by the breakpoint chlorination curve [54,144]. For values of chlorine to ammonia-nitrogen weight ratio ($\text{Cl}_2:\text{NH}_3\text{-N}$) lower than 5 g g^{-1} , the monochloramine is preferably formed. Between 5 g g^{-1} and 7.6 g g^{-1} , the monochloramine is transformed into dichloramine, while above this value, free chlorine and trichloramine increase.

Among the chloramines, monochloramine is preferably used due to its biocidal capacity, high stability (with a hydrolysis kinetic constant equal to $k = 0.076 \text{ h}^{-1}$ – Eq. 6), and almost no smell or odour [154]. Another advantage of monochloramine, compared to chlorine, is that its degradation produces nitrogen (Eq. 7), which can be released into the atmosphere without detriment to the environment [111].



The residual effect when applying chlorination depends on the so-called chlorine decay, which is an essential parameter for efficient and effective water treatment, particularly at the distribution stage, guaranteeing the best quality drinking water for consumers. The World Health Organization (WHO) recommends that free chlorine must be between 0.2 and 0.5 mg L^{-1} in drinking water for safety reasons [244].

However, a residual chlorine excess of 0.2 mg L^{-1} is difficult to maintain in the distribution system. Among the most relevant factors for this decay are organic impurities, oxidizable metal ions such as Fe(II) and Mn(II) , and nitrogen-containing compounds. However, when talking about distribution systems, the piping material must be considered since, if it is metallic, corrosion products may occur. These products can react with chlorine and lead to the formation of biofilms, made up of colonies of microorganisms. According to some authors, these biofilms are one of the main causes of chlorine overconsumption [48]. That said, there is a consensus that drinking water depends on treatment in the reservoirs of the treatment plants and in the distribution system; the consumption process in the former is faster and can take a few minutes but is easier to control; on the other hand, in the latter case, chlorine decay takes longer but, unlike the former, it is also more unpredictable [23,179]. In addition, the mass transport mechanism of chlorine in distribution pipes depends on the processes taking place in the bulk of the aqueous phase and near the walls of the pipes. The consumption of chlorine in these locations defines the so-called bulk and wall decays, respectively, and the sum of those two decays is the chlorine demand [228,236].

To have information on chlorine decays is, therefore, a key issue to guarantee a high level of water quality. Given the specificity of processes taking place in the pipeline wall and in the bulk, the corresponding kinetic processes are treated independently. Brown et al. [22] presented a comprehensive and thorough review article describing the different approaches for developing kinetic models [22]. For this reason, we will only refer here to the points we consider most relevant for assessment of chlorine decay.

The chlorine bulk decay is the one that comes closest to the decay in aqueous solution and, therefore, it would be expected that the reaction of chlorine with the different oxidizable compounds could follow a second-order kinetics [11,38]. However, most authors describe the decay kinetics of chlorine consumption as following a first-order kinetics [78]; i.e., the bulk kinetic rate constant, k_B , can be obtained through the dependence of the chlorine concentration, C , on time, t , according to the following equation:

$$C = C_0 e^{-k_B t} \quad (8)$$

where C_0 is the initial concentration of Cl_2 .

The reason for the use of this equation is essentially due to its simplicity and its ability to fit well to the experimental data due to the existence of a chlorine excess when compared to the oxidizable compounds [78]. However, if the two chlorination stages, described previously, are to be considered in different periods, then the Eq. (8) can be re-written by considering two processes in parallel, i.e.:

$$C = C_0[ze^{-k_{B1}t} + (1-z)e^{-k_{B2}t}] \quad (9)$$

where the rate constants k_{B1} e k_{B2} describe the fast and slow kinetic processes and z is the molar fraction of Cl_2 that has reacted in the fast process (1st stage). However, there is no consensus on these semi-empirical or even empirical equations, nor as to their universal nature or their dependence on the length of time chlorine remains in the distribution pipe.

The complexity of the process also comes from the fact that the kinetic constant is dependent on other variables, among which the most important are: a) initial Cl_2 concentration; b) temperature; c) organic matter; and d) rechlorination. Except for the dependence of k_B on temperature through the Arrhenius equation, the dependence of k_B on the other parameters is purely empirical, using power law equations [42, 120]; in fact, this type of equation is used to describe phenomena such as adsorption or the release of drugs from matrices [24,227]. Thus, if we consider that TOC is the physical quantity that best describes the content of NOM in water [209], an attempt to formulate an equation for predicting the kinetic decay constants was made by Hallam et al. [86] [86] using Eq. (10):

$$k_B = F \cdot e^{-E/RT} \cdot C_0^\alpha \cdot (NCl)^\beta (TOC)^\gamma \quad (10)$$

where F is a frequency factor, E is the activation energy, R is the gas constant, NCl is the re-chlorination number and α , β and γ are constants. However, as it should be expected given the number of fitting parameters, the correlation between Eq. (10) and experimental data is far from satisfactory [41]. This limitation in the prediction of k_B opens the door for this topic, as well as the one discussed below, to be the target and attention of the scientific community and engineers with an interest in drinking water treatment.

With regard to wall chlorine decay, k_W , this depends on the material and the possible corrosion reactions that can occur there, and the presence of biofilms or sediments. The simplest way to determine the contribution of the pipe walls to the chlorine decay is through the following equation:

$$k_W = k_T - k_B \quad (11)$$

where k_T is the total chlorine decay rate constant.

From the analysis of the kinetic rate constants published by various authors and summarized by Brown et al. [22], it can be concluded that the bulk decay rate constants can vary between 0.01 and 0.012 h^{-1} while the wall decay rate constants vary between 0 and 0.44 h^{-1} [22]. This possible higher value of k_W compared to k_B may be related to the characteristics of the pipes, such as their diameter, the material they are made of and their service life [7]. For example, for a new 150 mm diameter polyvinyl chloride pipe, $k_W \approx 1.25 \text{ d}^{-1}$, whilst for a pipe of the same diameter made of cement-lined cast iron, $k_W \approx 25 \text{ d}^{-1}$ [7].

3.2. Correlation of disinfection methods and DBPs formation

The literature on the correlation between disinfection methods and the formation of DBPs in drinking water is extensive and continuously evolving. Numerous studies have demonstrated that the type and amount of DBPs produced vary depending on the type of disinfection method, its operating conditions, and the initial water quality/composition [105]. These studies have enhanced the understanding of the influencing factors and mechanisms underlying DBP formation and

identified novel DBPs. Understanding these factors is critical for optimizing disinfection strategies and minimizing DBP formation in drinking water treatment systems, thereby ensuring the provision of safe, high-quality drinking water to the public [126].

Fig. 5 shows a simplified correlation between DBP precursors and disinfection method, indicating the formed classes of DBPs.

Chlorination yields THMs and HAAs as primary DBPs. The main factors influencing their formation include water temperature, pH, organic matter content and composition, chlorine dosage, contact time, and bromide ion concentration. For instance, THMs are more likely to form at water pH values higher than 7, while HAAs are formed in higher percentages at lower pH. The presence of free residual chlorine also allows the development of various reactions leading to the formation of DBPs, in particular THMs. Due to the efficiency and kinetics of the reactions involved, the formation of THMs can occur even in pre-breakpoint zones (after the addition of chlorine but with reduced oxidation effectiveness). Liu et al. [132] reported that in these pre-breakpoint zones, the formation of iodine-containing trihalomethanes (CHI_3 and CHClI_2) was still occurring although the reactivity of iodine is lower than that of chlorine and bromine [132].

Bromine- and iodine-containing species present in water bodies can, in fact, react with disinfectants, such as chlorine and chlorine dioxide, as well as with natural organic matter, leading to the formation of a wide range of DBPs. These Br-DBPs and I-DBPs generally exhibit greater cytotoxicity and genotoxicity than their chlorinated analogues [240, 264]. The origin of halogens in water is both natural and anthropogenic. Starting from the natural sources, the mineralization of water leads to natural occurring ions, as bromides and iodides, in the form of salts, whose concentrations in seawater can reach values as high as 67 mg L^{-1} and 8 $\mu\text{g L}^{-1}$, while in river water values as high as 10–20 mg L^{-1} and 0.5 mg L^{-1} , respectively [75,94,243,260]. The presence of halogens in soils, as constituents of e.g. clays, is also responsible for the dissolution of halogen ions in water. In addition to these sources, we must take into account the presence of halogens as a result of synthesis by organisms such as fungi and algae [27].

Regarding anthropogenic origins, the industrial and municipal WWTP discharges are an important source of salts/halogens in water [81], but these become very diluted in the main water streams (mainly rivers). Moreover, the chemical disinfection methods employed in drinking water treatment introduce halogens in significant amounts, in most cases chlorine. In fact, disinfection processes are the main source of halogens in treated water and, consequently, DBPs formation. Not only the occurrence of DBPs already regulated in worldwide regulations for drinking water quality, but also the emergence of unregulated and novel DBPs, have raised concerns about potential health risks.

The natural presence of anions I^- and Br^- in water leads to the formation of iodate and bromate by oxidation. Bromide is rapidly oxidized to hypobromous acid (HOBr) by HOCl , and HOBr reacts with NOM in either substitution or oxidation reactions. The HOBr reacts faster in a substitution reaction and more slowly in oxidation reaction, compared with HOCl or OCl^- [113,241]. The formation of Br-DBPs increases at higher bromide levels in chlorinated water. The use of chlorine also leads to the oxidation of iodide to hypoiodous acid (HIO), which, with subsequent oxidation by HOCl and HOBr/BrO^- , produces the iodate ion (IO_3^-) that is a non-toxic and stable compound. As a result, due to the low iodide level in natural water and to the oxidation of HOI to iodate, the formation of I-DBPs during chlorination of drinking water is often negligible. The oxidation of iodide to HIO is a very fast process with kinetic constants of $4.3 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$ and $2.4 \times 10^{10} \times [\text{H}_3\text{O}^+] \text{ M}^{-1} \text{ s}^{-1}$, when the oxidizing agent is HClO or NH_2Cl , respectively [19]. Finally, old solutions of sodium hypochlorite have been proven to lead to the formation of chlorite and chlorate, depending on the storage time and conditions [14,80].

Chlorine dioxide (ClO_2) leads to the formation of chlorite (ClO_2^-) and chlorate (ClO_3^-) as main DBPs, while THMs and HAAs are formed to a lesser extent than with free chlorine. The formation of chlorite and

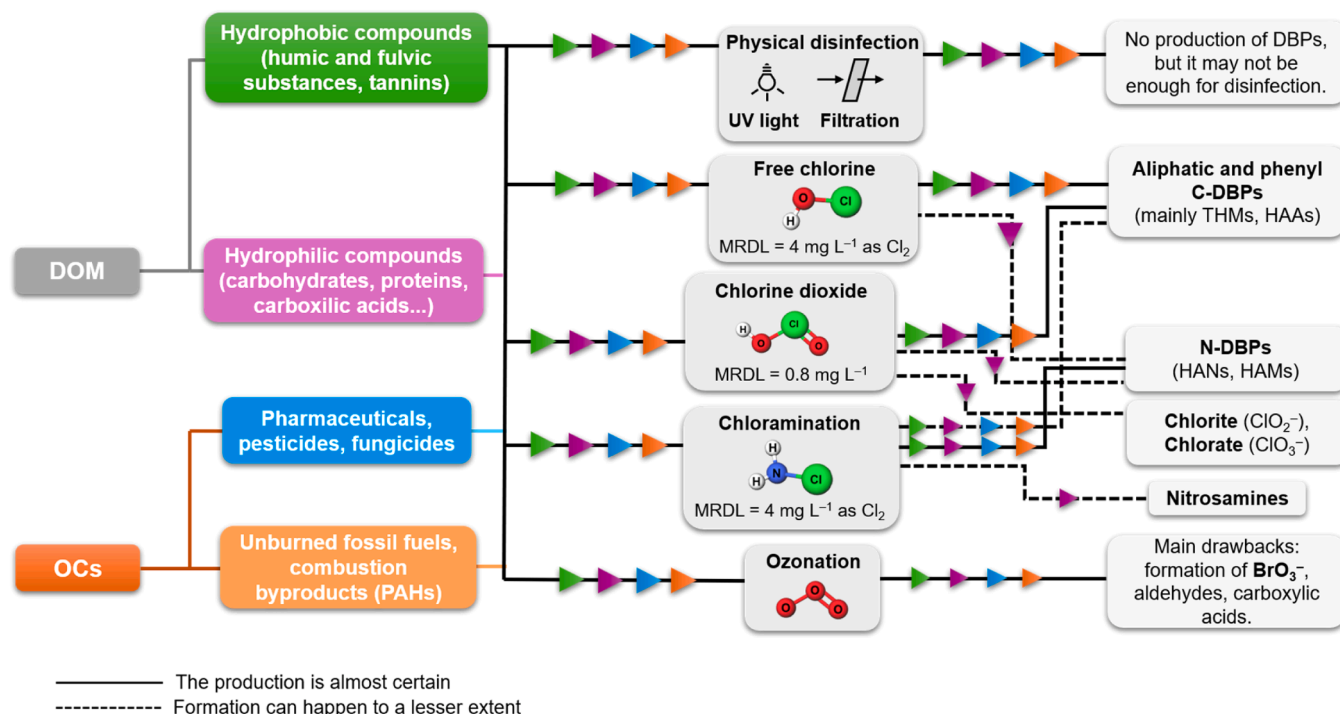


Fig. 5. – Interrelationship of water organic content, disinfection methods and potential formation of DBPs. MRDL corresponds to the maximum residual disinfection level mentioned by the United States Environmental Protection Agency (US EPA), for the disinfection method [246].

chlorate in drinking water primarily occurs through two mechanisms: (i) ClO_2 decomposition reactions, particularly in the presence of certain catalysts, reducing compounds or organic matter; (ii) oxidation of chlorite to chlorate, which is favoured under alkaline conditions and can be accelerated by higher temperatures and longer contact times. The main factors affecting DBP formation in this case are ClO_2 dosage, water quality parameters, as pH, temperature, the presence of chloride and bromide ions and organic matter content. The design and operation of water treatment systems, including factors such as mixing conditions, retention times, and disinfectant application methods, can also affect the formation of chlorite and chlorate [195].

Research efforts have focused on exploring alternative disinfection strategies, such as chloramination and ozonation, which may mitigate the formation of certain DBPs but can introduce other problems. However, there is some evidence that some DBP are still formed in chloramination resulting from reactions between NOM and small amounts of HOCl released via chloramine hydrolysis – reverse Eq. (3) [271]. Chloramination produces nitrosamines and nitrogen-containing DBPs, with formation influenced by ammonia and chlorine dosage, pH, temperature, and the presence of precursors like nitrogen-containing organic compounds. The nitrosamine that gets the most attention is NDMA, which is classified as a probable carcinogenic compound at concentrations of the order of ng L^{-1} . Therefore, while chloramination is generally considered to produce lower levels of regulated DBPs (THMs, HAAs) compared to chlorination, as already mentioned, it is still important to monitor and manage the formation of nitrosamines and other potential DBPs during water treatment processes to ensure water quality and safety. For instance, in the presence of chloramines, iodine cannot be oxidized to iodate, so HOI/OI^- will be able to react with NOM to form I-DBPs in chloraminated water [20,44,67]. The mechanisms of DBP formation are based on the assumption that chlorine, bromine and iodine atoms are incorporated in the NOM substrate sites, forming intermediate halogenated compounds before releasing the final products. The DBPs speciation depends on the intrinsic reaction kinetics of the corresponding intermediate with chlorine and bromine species [162, 187,258].

Ozonation's primary DBP is bromate (BrO_3^-) formed by ozone reaction with bromide in water. In this process, Br^- interacts with ozone to form OBr^-/HOBr , which can undergo several oxidation stages, either by the ozone or hydroxyl radicals ($\text{HO}\bullet$), leading to bromate (BrO_3^-) as the end product [66]. Bromate formation is still one of the main limiting factors in the application of ozonation, and the amount of ozone that can be dosed at the full-scale level due to the high toxicity of this byproduct. Moreover, ozone generates aldehydes and carboxylic acids as DBPs, affected by ozone dosage, pH, temperature, dissolved organic matter content, and reaction time.

Comprehensive studies evaluating the trade-offs between different disinfection methods, their effectiveness in reducing microbial load and their resulting DBPs profiles are still very scarce but crucial for informing water treatment practices and safeguarding public health. In fact, there is a growing emphasis on the health effects associated with exposure to DBPs and the development of risk assessment frameworks to evaluate the potential risks posed by these compounds.

4. Analytical detection and quantification of DBPs

It is crucial to monitor and analyse the DBPs to detect and tackle potential contamination issues, assist in remediation efforts, and ensure regulatory compliance with water quality standards. A few reviews on the quantification of DBPs, focusing on sample preparation and in chromatographic analysis for different DBP families have been published in recent years, including Huang et al. [97], and Yang et al. [259]; meanwhile Ma et al. [141], focused on these topics for HAAs only [141].

The next subsections will present the most commonly used analytical techniques for quantification of DBPs.

4.1. Colorimetric methods

The quantification of DBPs by colorimetric methods has mostly been aimed at the determination of THMs. These colorimetric methods are usually based on the Fujiwara's reaction. In this reaction, the THMs are transferred to pentane by a liquid-liquid extraction (LLE), after which

the pentane phase is heated with pyridine and sodium hydroxide to form a pink/red complex, which can then be read by UV-Vis spectrophotometry [160]. This method, however, requires some caution in its application as the pyridine is a hazardous compound. Additionally, as it is a colorimetric detection technique, the quantification of individual THMs in a mixed THMs solution is not possible. Therefore, only the total THMs concentration in water can be determined. This shows the poor selectivity of colorimetric methods which makes their application to complex sample matrices and, consequently, real drinking water samples a challenge. Furthermore, the results of colorimetric methods are also very dependent on matrix interferences. For these more complex samples, chromatographic methods should be used for more accurate results.

An attempt to assess the method's performance for the determination of BDCM was carried out by the authors from University of Coimbra (Figure S1 of the [Supplementary Material](#)). It was observed that the pyridine-BDCM complex was formed; however, in terms of quantification, readings at 530 nm showed that linearity was only achieved for solutions with concentrations higher than 5 mg L^{-1} , a concentration superior to the legislation maximum value established for the BDCM ($60 \text{ } \mu\text{g L}^{-1}$ by [245]). The complex formation was also attempted with the substitution of pyridine by imidazole, the advantage of this substitution being the possible determination of the complex by fluorescence to increase resolution. However, the imidazole substitution did not lead to the formation of a complex with BDCM. This demonstrates that colorimetric methods still present high detection limits to be applied to real drinking water samples. However, recent studies have been made to improve their sensitivity for lower concentrations (e.g. for heavy metals) [33].

More recently, Zhong et al. [276] developed a colorimetric method for the detection of a HAN, the dichloroacetonitrile (DCAN). The formation of a complex between the HAN and copper species was observed, which is then extracted with chloroform and turned visible by dithizone. This method was based on measuring the fluorescence of Cu^{+} -dithizone complex. It showed a good performance for the DCAN, trichloroacetonitrile (TCAN), bromochloroacetonitrile (BCAN) and dibromoacetonitrile (DBAN), allowing the quantification of solutions in the $\mu\text{g L}^{-1}$ range [276].

4.2. Chromatographic methods

4.2.1. Sample preparation techniques for extraction of DBPs

Most chromatographic methods employed for quantification of DBPs require a preparation of the samples prior to their detection. There are several sample preparation techniques available for the extraction of DBPs, including LLE, purge and trap (P&T), and SPE [6,71,197]. The use of the different sample preparation techniques depends greatly on the volatility of the DBPs; THMs, HKs, HNMs, HANs are considered as volatile DBPs, whereas HAAs and halobenzoquinones are considered non-volatile DBPs [250,233].

In the case of LLE, solvents such as pentane and methyl-tert-butyl ether (MTBE) are usually used with the addition of NaCl and/or Na_2SO_4 to increase the extraction efficiency [222]. In some cases, however, such as the case of HAAs, derivatization is combined with LLE to make them more suitable for detection, as the HAAs are transformed into their corresponding methyl esters which are then extracted to an organic solvent prior to detection [237]. With this, it is possible to reduce the acidity of the HAAs, increase their volatility and thermal stability, contribute to an increase of its molecular weight or introduce functional groups that improve both the specificity and sensitivity, favouring the detection. There is a wide variety of derivatization agents that can be used for this purpose, depending on the type of detector coupled with the GC, including bis(trimethylsilyl)trifluoroacetamide (BSTFA), pentafluorobenzylhydroxylamine, methanol, or methanol combined with MTBE [108,135]. Additionally, when applying methylation, salting-out (with NaCl and Na_2SO_4) can also be performed to

improve the extraction efficiency [237]. Other more recent techniques with a similar technology of LLE have been developed, such as dispersive liquid-liquid micro extraction (DLLME), micro liquid-liquid extraction (MLLE) and directly suspended droplet microextraction (DSDME) allowing a miniaturization of classic liquid-liquid extraction [180]. These techniques allow the reduction of both the amount of solvents used and the amount of treated sample.

In P&T the solution is placed in a closed vial with one inlet, that allows for as inert gas to enter the vial, and an outlet, from which the headspace is continuously removed, and forced to pass through an adsorbent, that traps the analyte, which is then desorbed during the detection. This technique can aid in the quantification of low concentration solutions, however, it cannot be automatized and is time-consuming [1,103].

The SPE method takes advantage of the adsorption ability of a solid to adsorb the target analyte, however, conventional SPE is usually a time-consuming alternative, with a high solvent consumption [103]. In SPE, the type of solid phase, type and amount of elution solvents, speed and pressure of elution must be appropriately selected [18,278]. Before applying the sample, it is important to condition the solid phase with the solvent used to elute the analytes. After applying the appropriate amount of sample, the solid phase is washed to remove unwanted matrix components. The analytes are then eluted using an organic solvent; after the elution, derivatization or a concentration step may be required by evaporating the diluter [278]. Smaller-scale techniques similar to SPE can also be used, such as microextraction by packed sorbent with programmed temperature vaporizer (MEPS-PTV).

The solid-phase microextraction (SPME) sample preparation technique is based on the equilibrium of analytes between the solid extraction phase (normally a coated fibre) and the extracted matrix (liquid or gas). It is cost-effective and environmentally friendly. It is necessary to optimize various experimental parameters that affect the extraction efficiency, such as the coating material of the fibre, volume to liquid headspace (HS), extraction time, extraction temperature, salt addition, stirring, etc. according to the detailed experimental protocol presented in Risticic et al. [185]. Due to the properties of volatile DBPs, the HS system is appropriate for their extraction, where, at the optimized extraction time and temperature, analytes are transferred from the water phase to the gas phase, which is injected directly onto the GC system [5]. A common approach is to combine HS with SPME, thus HS-SPME is a popular extraction technique for analysis of water samples [26,173]. In such a system, the analytes transferred to the gas phase are sorbed by the fibre, e.g., coated with polydimethylsiloxane (PDMS). In the next step, they are desorbed in the presence of an inert gas and high temperature and transferred to a GC system. The hollow-fibre liquid phase microextraction (HF-LPME) technique can also be used to increase the efficiency of analyte sorption, in which a hollow-fibre is soaked in an extractive organic solvent. Such systems most often use polypropylene hollow-fibre saturated in octanol, and modifications of polypropylene hollow-fibre with carbon sorbents such as graphene or carbon nanotubes can also be used [53,247].

Microextraction techniques are gaining more attention and novel alternatives are being developed due to their numerous advantages over traditional techniques. The former do not require the use of organic solvents, use smaller sample sizes, resulting in an increase of the method's sensitivity and minimization of interferences; they are also relatively easy to use. These include SPME-arrow, high capacity sorptive extraction (HiSorb), stir bar sorptive extraction (SBSE), and thin-film SPME (TF-SPME) [137]. The latter three techniques require a thermal desorption unit followed by GC-MS (TD-GC-MS), while SPME and SPME-arrow need only GC-MS. The SBSE technique provides a larger volume of adsorbent material ($24 \text{ } \mu\text{L}$) and increased surface capacity (154 mm^2) [56]. It mainly uses PDMS, which has a low affinity for compounds of medium and high polarity ($\log K_{\text{OW}} < 3$) [168]. Another available coating for SBSE is that of PDMS/ethylene glycol. On the other hand, TF-SPME ($9 \text{ } \mu\text{L}$, 190 mm^2) offers various adsorbent coatings

(PDMS, PDMS/divinylbenzene – PDMS/DVB, PDMS/Hydrophilic Lipophilic Balanced – PDMS/HLB, Carboxen/PDMS – CAR/PDMS) with a higher affinity for polar compounds compared to PDMS. HiSorb is more advanced (65 μL , 96.1 mm^2) and robust compared to traditional SPME. However, only four commercial adsorbents are available in HiSorb (PDMS, PDMS/Carbon wide range – PDMS/CWR, PDMS/DVB, and DVB/CWR/PDMS). On the other hand, traditional SPME fibres have a smaller capacity of 0.6 μL and a surface area of 9.4 mm^2 , but they have a larger variety of commercial adsorbents available [56,168].

It should be noted that these different sample preparation methods must be optimized depending on the DBP to be analysed and type of sample, as recovery, solvent consumption, analysis time varies significantly. More recently, a particular attention has been given to greener sample preparation techniques which includes ten main principles, including the (1) favouring of in situ sample preparation, (2) usage of safer solvents and reagents, (3) targeting sustainable, reusable and renewable materials, (4) minimization of waste, (5) minimization of sample, chemical and material amounts, (6) maximization of sample throughput, (7) integration of steps and promotion of automation, (8) minimization of energy consumption, (9) choice of the greenest possible post-sample preparation configuration for analysis and (10) insurance of safe procedures for the operator [136].

4.2.2. GC-MS

Table 1 presents a compilation of the works in literature that used GC-MS to measure volatile DBPs. The detailed conditions of the quantification methods used in literature are presented in Table S1 of the Supplementary Material. The limits of detection (LOD) and quantification (LOQ) reported for volatile DBPs are strongly influenced both by DBP family and by the applied sample preparation strategy, reflecting differences in volatility, polarity, and chemical stability, which are often pH-dependent. THMs, the most extensively studied DBP family, consistently show lower LODs when enrichment techniques such as SPE or HS-SPME are employed, reaching sub-ng L^{-1} levels (e.g., 0.0004–0.0013 $\mu\text{g L}^{-1}$ with SPE-GC-MS in Wang et al. [230]), compared to LLE, which frequently reports higher LOQs [46,160,230]. This trend highlights the superior preconcentration efficiency and reduced solvent dilution associated with microextraction approaches, particularly for hydrophobic THMs. HKs and HANs, which are more chemically reactive and sensitive to hydrolysis under neutral to alkaline pH, are predominantly analysed using HS-SPME or LLE, often resulting in higher or undefined LODs [161,205], indicating analytical challenges related to instability during sample handling. HNMs, though less frequently studied, show comparatively higher LODs, especially when single-drop HS-SDME and LLE GC-MS are applied [128,150], suggesting limitations in mass transfer and extraction reproducibility.

Across all DBP families, coupling GC with mass spectrometric

Table 1 –
Parameters of GC-MS to quantify volatile DBPs.

Analyte	Analysis Method	LOD ($\mu\text{g L}^{-1}$)	LOQ ($\mu\text{g L}^{-1}$)	Recovery Rate (%)	Relative Standard Deviation (%)	Analysis Time (min)	Reference
Trihalomethanes (THMs)							
TCM, TBM, BDCM, DBCM	LLE GC-MS	<i>n.d.</i>	<i>n.d.</i>	78–138.4	37.9–3.4	~36	[160]
TCM, TBM, BDCM, DBCM	LLE GC-MS	<i>n.d.</i>	0.050	81–129	2–16	~13	[46]
TCM, TBM, BDCM, DBCM	P&T GC-MS	<i>n.d.</i>	<i>n.d.</i>	91.3–126	8–17	16	[26]
TBM, BDCM, DBCM	SPE GC-MS	0.0004–0.0013	0.0012–0.0043	86.0–114.2	1.36–3.18	12	[230]
TCM, TBM, BDCM, DBCM	SPE GC-MS	<i>n.d.</i>	0.050	81–129	2–16	~13	[46]
TCM, TBM, BDCM, DBCM	HS-SPME	0.01–0.02	0.05–0.50	81–115	1.4–9.3	15	[257]
TCM, TBM, BDCM, DBCM	GC-MS	0.01, 0.01, 0.003, 0.003	<i>n.d.</i>	<i>n.d.</i>	< 13	27	[142]
TCM, TBM, BDCM, DBCM	HS-SPME	<i>n.d.</i>	<i>n.d.</i>	91–120	5–17	16	[166]
TCM, TBM, BDCM, DBCM	GC-MS	<i>n.d.</i>	<i>n.d.</i>	95–98	5.2–6.3	~25	[152]
TCM, TBM, BDCM, DBCM	HS GC-MS	0.01, 0.01, 0.015, 0.02	<i>n.d.</i>	95–98	5.2–6.3	~25	[152]
Haloketones (HKs)							
1,1-DCA, CA, 1,1,1-TCA, 1,1-DBA, 1-B–1,1-DCA, 1,3-DCA, 1,1,3-TCA, 1,1,3,3-TeCA, 1,1,3,3-TeBA	LLE GC-MS	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	44–58	[8]
1,1-DCA, 1,1,1-TCA, 1,3-DCA	LLE GC-MS	<i>n.d.</i>	<i>n.d.</i>	66.2–121.6	1.3–35.1	12	[161]
1,1-DCA, CA, 1,1,1-TCA, 1,1-DBA, 1-B–1,1-DCA, 1,3-DCA, 1,1,3-TCA, 1,1,3,3-TeCA, 1,1,3,3-TeBA	LLE GC-MS	<i>n.d.</i>	0.1	30–110	0.2–30	47–49	[46]
1,1-DCA, 1,1,1-TCA	HS-SPME	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	2–18	27	[142]
1,3-DCA, 1,1-DCA, 1,1-DBA, 1,1,3-TCA, 1,1,1-TCA, 1,1-DB–3-CA, 1,1,3-TBA, 1,1,1-TBA, 1,1,3,3-TeCA, 1,1,1,3-TeCA, 1,1-DB–3,3-DCA, 1,3-DB–1,3-DCA, 1,1,3-TB–3-CA	GC-MS	<i>n.d.</i>	<i>n.d.</i>	92–99	5.4–8.2	12.3–27	[205]
1,1-DCA, 1,1,1-TCA	HS-SPME	0.1–0.18	<i>n.d.</i>	<i>n.d.</i>	4–7	30	[107]
1,1-DCA, 1,1,1-TCA	GC-MS	<i>n.d.</i>	<i>n.d.</i>	<i>n.d.</i>	4–7	30	[107]
Halonitromethanes (HNMs)							
CNM, DCNM, TCNM, BNM, BCNM, BDCNM, DBNM, DBCNM, TBNM	HS GC-MS	0.15, 0.04, 0.03, 0.16, 0.06, 0.07, 0.08, 0.11, 0.6	<i>n.d.</i>	94–96	6.0–7.0	20	[151]
CNM, DCNM, TCNM, BNM, BCNM, DBNM	HS GC-MS	0.13, 0.04, 0.03, 0.14, 0.06, 0.08	<i>n.d.</i>	95–98	~5.6	20	[152]
CNM, DCNM, TCNM, BNM, BCNM, BDCNM, DBNM, DBCNM, TBNM	HS-SDME	0.9, 0.07, 0.06, 0.9, 0.08, 0.2, 0.9, 0.3, 1.2	<i>n.d.</i>	93–95	6.2–13.2	<i>n.d.</i>	[150]
BCNM, DCNM, BDCNM, DBCNM, TBNM, TCNM	GC-MS	0.09, 0.2, 1, 2, 6, 0.08	<i>n.d.</i>	> 90	7–43	41	[128]
Haloacetonitriles (HANs)							
MCAN, DCAN, TCAN, MBAN, BCAN, DBAN	LLE GC-MS	0.09, 0.2, 1, 2, 6, 0.08	<i>n.d.</i>	> 90	7–43	41	[128]
MCAN, DCAN, TCAN, MBAN, BCAN, DBAN	HS GC-MS	0.15, 0.03, 0.03, 0.2, 0.05, 0.05	<i>n.d.</i>	95–98	~5.6	20	[152]

n.d.: value not defined

detection significantly enhances selectivity and sensitivity relative to conventional detectors, enabling reliable identification at trace levels even in complex water matrices. However, the variability in reported LODs underscores that detector performance alone cannot compensate for suboptimal or complex sample preparation.

Overall, THMs remain the most intensively investigated DBPs due to their regulatory relevance and analytical accessibility, whereas emerging DBP classes such as HNMs and HKs remain underrepresented, largely because their chemical behaviour complicates low-level detection despite advances in GC-MS instrumentation.

Table 2 presents a compilation of the works in literature that used GC-MS to measure non-volatile DBPs. The detailed conditions of the quantification methods used in literature are presented in Table S2 of the Supplementary Material. The LOD and LOQ values reported for non-volatile DBPs analysed by GC-MS are strongly governed by DBP family characteristics and sample preparation strategies, reflecting differences in polarity, acidity, and pH-dependent speciation. HAAs, the most extensively studied non-volatile DBPs due to their regulatory relevance and acidic nature, exhibit a wide variability in the obtained sensitivity depending on extraction and derivatization efficiency, with SPE and miniaturized liquid extraction approaches generally providing lower LODs (as low as 0.009 $\mu\text{g L}^{-1}$ in Waseem and Abdullah [237]) compared to conventional LLE and SDME, which often result in higher or poorly defined LOQs [199,237,255]. This reflects the strong influence of pH control during sample preparation, as incomplete protonation of HAAs at inappropriate pH can significantly reduce extraction efficiency. Advanced inlet and detection configurations, such as MEPS-PTV coupled with tandem MS, improve selectivity but do not necessarily yield lower LODs, indicating that preconcentration remains the dominant sensitivity-limiting step [70,109]. In contrast, HAMs were sparsely investigated and primarily analysed using LLE, resulting in comparatively high LODs (up to 2 $\mu\text{g L}^{-1}$ for BACAm in Liew et al. [128], highlighting analytical challenges associated with their polarity and hydrolytic instability [128]. HPs show the lowest LODs among non-volatile DBPs when sorptive techniques such as SBSE-TD or optimized SPME are employed, reaching sub-ng L^{-1} levels (0.001–0.002 $\mu\text{g L}^{-1}$ in Kawaguchia et al. [106]; 0.0002–0.009 $\mu\text{g L}^{-1}$ in Wang et al. [235]), owing to their strong affinity for nonpolar sorbents and enhanced detector response [106,235].

Overall, GC-MS significantly improves the detection of structurally diverse non-volatile DBPs; however, sensitivity is ultimately dictated by the compatibility between DBP chemistry, pH-adjusted sample preparation, and extraction mechanism, explaining why HAAs and HPs show advantage over HAMs and other emerging non-volatile DBPs that remain underexplored.

HAMs have not been widely measured by GC-MS probably because their non-volatile character requires a prior derivatization when applied. HPs are another family of non-volatile DBPs that require sample derivatization, being in this case more explored, usually performed with dichloromethane (DCM), methyl iodide, BSTFA, pentafluoropyridine and acetic anhydride, as seen in Table S2 of the Supplementary Material.

4.2.3. GC-ECD

The GC-electron capture detection (GC-ECD) technique that requires two columns, one for quantification and the other for verification, was already used to determine compounds that belong to THMs, HKs and HNMs groups of DBPs. A recent improvement on ECD relies on the μECD detector, where the detector presents a smaller internal volume, allowing a better separation efficiency and higher sensitivity. In Table 3, examples of the use of this technique for the determination of volatile DBPs in water samples are presented. The detailed conditions of the quantification methods used in literature are presented in Table S3 of the Supplementary Material.

The LOD and LOQ values reported for volatile DBPs using GC-ECD are strongly dependent on both DBP family and sample preparation approach, reflecting the high halogen selectivity but limited structural

Table 2 –
LOD and LOQ of the use of GC-MS to quantify non-volatile DBPs.

Analyte	Analysis Method	LOD ($\mu\text{g L}^{-1}$)	LOQ ($\mu\text{g L}^{-1}$)	Reference
Haloacetic acids (HAAs)				
MCAA, DCAA, TCAA, MBAA, DBAA, TBAA, BCAA, BDCAA, CDBAA	HS-SPME GC-MS/IT	0.01–0.45	0.2–1.5	[200]
MCAA, DCAA, TCAA, MBAA, DBAA, TBAA, BCAA, BDCAA, DBCAA	LLE GC-MS	0.04–0.83	<i>n.d.</i>	[255]
MCAA, DCAA, TCAA, MBAA, DBAA, BCAA	SDME GC-MS	0.1–1.2	0.5–5	[199]
MCAA, DCAA, TCAA, MBAA, DBAA, BCAA, TBAA, BDCAA, DBCAA	SPE GC-MS	0.009–0.42	0.02–1.26	[237]
MCAA, DCAA, TCAA, MBAA, DBAA	MEPS-PTV GC-MS/ MS	0.36–1.2	<i>n.d.</i>	[70]
MCAA, DCAA, TCAA, MBAA, DBAA	DLLME GC-MS	<i>n.d.</i>	0.05	[9]
MCAA, DCAA, TCAA, MBAA, DBAA, BCAA, TBAA, BDCAA, DBCAA, CIAA, BIAA, DIAA, MIAA	MLLE GC-MS	0.01–0.4	0.03–1.5	[30]
MCAA, DCAA, TCAA, MBAA, DBAA, BCAA, TBAA, BDCAA, DBCAA, DIAA, MIAA	SPE GS-MS/MS	<i>n.d.</i>	0.01–0.5	[109]
MCAA, DCAA, TCAA, MBAA, DBAA, BCAA, TBAA, BDCAA, DBCAA	LLE GC-MS	0.01–1.8	0.3–3.9	[72]
Haloacetamides (HAMs)				
BACAm, CACAm, DBACAm, DCACAm, TCACAm	LLE GC-MS	2, 1, 0.1, 0.08, 0.1	<i>n.d.</i>	[128]
Halophenols (HPs)				
2,4-DCP, PCP	HF-LPME GC-MS	0.014–0.015	0.022–0.026	[15]
2-CP, 4-CP, 2,4-DCP, 3,4-DCP, 2,3,5-TCP, 4-BP, 4Cl3Me	SPE GC-MS/IT	0.002–0.016	0.05	[112]
2,4-DCP, 2,4,6-TCP; 2,3,4,6-TeCP, PCP	SBSE-TD GC-MS	0.001–0.002	0.005–0.01	[106]
2-CP, 2,4-DCP, 2,4,6-TCP, PCP, 2,4-DMP, 4Cl3Me	SBSE-TD GC-MS	0.1–0.4	<i>n.d.</i>	[149]
2-CP, 4-CP, 2,4-DCP, 2,6-DCP, 2,4,5-TCP, 2,4,6-TCP, 2,3,4,6-TeCP, 4Cl3Me, PCP	SPME GC-MS	0.052–4.1	0.16–12	[210]
2-CP, 2,4 DCP, 2,4,6 TCP, 2-BP, 2,4- DBPh, 2,4,6-TBP	SPME GC-MS	0.0002–0.009	0.0008–0.003	[235]

(continued on next page)

Table 2 – (continued)

Analyte	Analysis Method	LOD ($\mu\text{g L}^{-1}$)	LOQ ($\mu\text{g L}^{-1}$)	Reference
2-BP, 4-BP, 9-BP, 2,3-DBPh, 2,4-DBPh, 2,5-DBPh, 2,6-DBPh, 3,4-DBPh, 3,5-DBPh, 2,3,4-TBP, 2,3,5-TBP, 2,3,6-TBP, 3,4,5-TBP, 2,3,4,5-TeBP, 2,3,4,6-TeBP, 2,3,5,6-TeBP, PBP	LLE GC-MS	0.39–1.26	0.5	[131]

n.d.: value not defined

Table 3 –

LOD and LOQ of the use of GC-ECD to quantify volatile DBPs.

Analyte	Analysis Method	LOD ($\mu\text{g L}^{-1}$)	LOQ ($\mu\text{g L}^{-1}$)	Reference
Trihalomethanes (THMs)				
TCM, TBM, BDCM, DBCM	LLE GC-ECD	n.d.	n.d.	[222]
TCM, TBM	DSDME GC-ECD	0.112–0.128	0.373–0.425	[180]
TCM, TBM, BDCM, DBCM	HF-LPME GC- μ ECD	0.010–0.035	0.012–0.067	[53]
TCM, TBM, BDCM, DBCM	HF-LPME GC- μ ECD	0.01–0.10	0.03–0.17	[247]
TCM, TBM, BDCM, DBCM	HS GC- μ ECD	0.09–0.14	0.32–0.47	[5]
TCM, TBM, BDCM, DBCM	HS-SPME GC- μ ECD	0.01–0.03	0.03–0.08	[26]
Haloketones (HKs)				
1,1-DCP, 1,1,1-TCP	LLE GC-ECD	n.d.	n.d.	[222]
Halonitromethanes (HNMs)				
TCNM	LLE GC-ECD	n.d.	n.d.	[222]
Haloacetonitriles (HANs)				
BCAN, DBAN, DCAN, TCAN	LLE GC-ECD	n.d.	n.d.	[222]

n.d.: value not defined

specificity of the detector. For THMs, which dominate the literature in Table 3, microextraction techniques such as HF-LPME and HS-SPME yield very low LODs (down to $0.010 \mu\text{g L}^{-1}$); for classical LLE, the sensitivity parameters are not disclosed [53,222,247]. This can be attributed to enhanced analyte enrichment and reduced solvent background, which are particularly beneficial for ECD due to its susceptibility to matrix interferences. DSDME provides moderate sensitivity for THMs (LOD ≈ 0.11 – $0.13 \mu\text{g L}^{-1}$), indicating that extraction efficiency and phase stability remain limiting factors [180]. In contrast, HKs, HNMs, and HANs are sparsely investigated with GC-ECD and are almost exclusively analysed using LLE methods, largely following standardized protocols [222], resulting in unreported LODs and LOQs. This gap reflects both the chemical instability of these DBPs and the inability of ECD to compensate for losses occurring during sample preparation. Although GC-ECD offers excellent sensitivity for halogenated compounds, its lack of molecular confirmation compared to GC-MS limits its applicability for emerging DBPs.

The GC-ECD technique can be used to determine non-volatile DBPs in a water matrix after appropriate sample preparation (Table 4). The detailed conditions of the quantification methods used in literature are presented in Table S4 of the Supplementary Material. The performance of GC-ECD for the determination of non-volatile DBPs is strongly modulated by DBP family, halogen content, and the efficiency of the applied sample preparation method, with pH control playing a decisive

Table 4 –

LOD and LOQ of GC-ECD to quantify non-volatile DBPs.

Analyte	Analysis Method	LOD ($\mu\text{g L}^{-1}$)	LOQ ($\mu\text{g L}^{-1}$)	Reference
Haloacetic acids (HAAs)				
BCAA, BDCAA, CDBAA, DBAA, DCAA, MBAA, MCAA, TBAA, TCAA	LLE GC-ECD	0.01–0.02	0.05–0.50	[223]
Haloacetamides (HAMs)				
BCAcAm, TCACAm, DBAcAm, ClAcAm, BDCAcAm, BIAcAm, DBCAcAm, TBACAm, DIACAm, DCACAm	SPE GC-ECD	0.003, 0.002, 0.002, 0.003, 0.002, 0.003, 0.003, 0.003, 0.003, 0.002	0.010, 0.005, 0.005, 0.010, 0.005, 0.010, 0.010, 0.010, 0.010, 0.005	[278]
Chlorophenols (CPs)				
3,5-DCP, 2,3-DCP, 2,3,5-TCP, 2,4,5-TCP, 2,3,5,6-TeCP, PCP	SPE GC-ECD	6.6, 6.2, 4, 2.6, 2.9, 0.5	n.d.	[18]

n.d.: value not defined

role for acidic species.

For HAAs, classical LLE coupled to GC-ECD yields relatively low LODs (0.01 – $0.02 \mu\text{g L}^{-1}$) and moderate LOQs (0.05 – $0.50 \mu\text{g L}^{-1}$), as reported in standardized protocols [223], reflecting the strong electron-capturing response of halogenated acids once adequately protonated under acidic conditions. HAMs exhibit substantially improved sensitivity when SPE is employed, achieving LODs as low as 0.002 – $0.003 \mu\text{g L}^{-1}$ [278], which underscores the importance of selective sorbents to overcome their higher polarity and pH-dependent hydrolytic instability. CPs, despite being strongly halogenated, show markedly higher LODs (0.5 – $6.6 \mu\text{g L}^{-1}$) even when SPE is applied [18], indicating limitations associated with sorbent–analyte interactions and possible matrix suppression effects in ECD detection.

Overall, while GC-ECD provides excellent sensitivity for highly halogenated non-volatile DBPs, its effectiveness is highly contingent upon optimized sample preparation and chemical speciation control, which explains why HAAs and HAMs, having the sample preparation protocols developed, are more frequently and reliably quantified than chlorophenols, despite the latter's intrinsic electron-capturing properties. However, it should be noted that the representativeness of the data is low due to the scarcity of works in this domain.

4.2.4. LC-MS

While GC-MS is widely applied for analysis of (semi)volatile DBPs, it is not suitable for polar and high molecular weight DBPs, since these DBPs are hardly extractable from the aqueous phase and are not volatile enough for GC analysis [279]. Therefore, LC-MS is becoming increasingly important for the identification and quantification of known and unknown DBPs. The reversed-phase LC (RPLC) and the electrospray ionization (LC-ESI) are the most common chromatographic separation and ionization methods, respectively [259]. Other ionization techniques like atmospheric pressure chemical ionization are rarely used but can be applied for analysis of less polar DBPs like HAMs [37].

Table 5 presents a compilation of the works in the literature that used LC-MS to measure non-volatile DBPs. The detailed conditions of the quantification methods used in literature are presented in Table S5 of the Supplementary Material.

Despite the wide application of reversed-phase LC-MS in various DBP studies, this method can result in a significant analytical gap by overlooking the very polar fractions of DBPs, as these compounds are hardly

Table 5 –
LOD and LOQ of LC-MS to quantify non-volatile DBPs.

Analyte	Analysis Method	LOD ($\mu\text{g L}^{-1}$)	LOQ ($\mu\text{g L}^{-1}$)	Reference
Haloacetic acids (HAAs)				
MCAA, DCAA, TCAA,	LC-ESI-MS	0.024–0.118	<i>n.d.</i>	[216]
MBAA, DBAA,	LC-ESI-MS	0.06–0.16	0.18–0.48	[55]
BCAA, BDCAA,	LC-ICP-	0.8–1.6	4.6–12	[121]
CDBAA, TBAA	MS/MS			
DCAA	LC-ESI-MS	1	5	[52]
MCAA, DCAA, TCAA,	LC-ESI-	0.03–3	0.06–6	[175]
MBAA, DBAA,	HRMS			
BCAA, BDCAA,				
DCBAA, TBAA,				
MIAA, BIAA, CIAA,				
DIAA				
MCAA, DCAA, MBAA,	LC-ESI-MS	0.05–0.1	<i>n.d.</i>	[4]
BCAA, DBAA				
MCAA, DCAA, TCAA,	LC-ESI-MS	0.01–0.6	0.5–2	[174]
MBAA, DBAA,				
BCAA, BDCAA,				
CDBAA, TBAA,				
MIAA, DIAA				
MCAA, MBAA, MIAA,	RPLC-	0.05–2	0.15–6.7	[232]
DCAA, DBAA, DIAA,	HRMS			
TCAA, BDCAA,				
CDBAA, TBAA				
MCAA, DCAA, TCAA,	SPE LC-	0.04–0.3	0.12–1.05	[177]
MBAA, DBAA	ESI-MS			
MCAA, DCAA, TCAA,	LLE LC-	0.1–0.5	<i>n.d.</i>	[156]
MBAA, DBAA,	ESI-MS/			
BCAA, BDCAA,	MS			
CDBAA, TBAA				

n.d.: value not defined

retained on reversed-phase columns (e.g., C18) [182]. For the case of HAAs specifically, there is a wider application of the LC-ESI coupled with the MS detector, despite similar LOD and LOQ values being achieved (see Table 5). Prieto-Blanco et al. [177] and Murakami et al. [156] also performed a prior sample preparation to the application of the LC-ESI-MS based on SPE and LLE, where for the SPE similar LOD and LOQ values were achieved when compared to LC-ESI without sample preparation. For the case of using LLE combined with LC-ESI-MS, the LOD and LOQ for the HAAs were higher in one order of magnitude [156, 177].

Another alternative to RPLC-MS is LC with inductively coupled plasma and MS (LC-ICP-MS) which aims to be less prone to matrix effects, avoiding the need for internal standards, generally independent of molecular structure, being, overall, a more robust technique [121]. However, when comparing the Lajin and Goessler [121] study, where LC-ICP-MS was used for the quantification of several HAAs, to other studies with LC-ESI-MS present in Table 5, it can be verified that the LOD and LOQ values are higher when using ICP-MS.

More recently, to overcome the challenge in retaining the polar DBPs into the reversed-phase columns, alternative chromatographic separation methods, like hydrophilic interaction liquid chromatography (HILIC) and supercritical fluid chromatography (SFC), were tested to narrow such analytical gaps [159,266].

4.2.5. IC-MS and IC-CD

Table 6 provides an overview of analytical methods based on IC, specifically IC-MS and ion chromatography coupled with conductivity detection (IC-CD), used to detect non-volatile DBPs. Unlike GC and LC, IC is particularly suited for analysing ionic and polar species in aqueous samples. The detailed conditions of the quantification methods used in literature are presented in Table S6 of the Supplementary Material. Various IC techniques have been employed for the detection of halides and HAAs in water samples. Chloride (Cl^-) and bromide (Br^-) are commonly analyzed using IC-CD, with different column setups and eluents to optimize sensitivity [58].

Table 6 –
LOD and LOQ of IC-MS, IC-CD and IC-UV to quantify non-volatile DBPs.

Analyte	Analysis Method	LOD ($\mu\text{g L}^{-1}$)	LOQ ($\mu\text{g L}^{-1}$)	Reference
Cl^- , Br^-	IC-CD	<i>n.d.</i>	<i>n.d.</i>	[191]
MCAA, DCAA,	IC-CD	3.39, 4.87,	11.28, 16.23,	[140]
TCAA, Cl^- , Br^-		6.81, 0.06, 2.14	22.71, 0.21,	
			7.12	
MCAA, DCAA,	HPIC-MS/	0.05, 0.01, 1,	0.1, 0.02, 2,	[256]
TCAA, BrO_3^- ,	MS	0.01, 0.1, 0.01,	0.02, 0.2,	
Br^- , MBAA,		0.02, 0.01	0.02, 0.05,	
DBAA, TBAA			0.02	
MCAA, MBAA,	IC-ESI-MS	<i>n.d.</i>	<i>n.d.</i>	[225]
DCAA, TCAA,				
DBAA, BCAA,				
BDCAA,				
CDBAA, TBAA				
Chlorite, MCAA,	IC-ESI-	0.036, 0.134,	0.110, 0.405,	[25]
MBAA, MIAA,	MS/MS	0.026, 0.045,	0.078, 0.136,	
Bromate,		0.042, 0.059,	0.127, 0.177,	
DCAA, BCAA,		0.037, 0.055,	0.111, 0.166,	
DBAA, CIAA,		0.085, 0.188,	0.256, 0.569,	
Chlorate,		0.036, 0.113,	0.109, 0.342,	
DIAA, TCAA,		0.099, 0.108,	0.301, 0.326,	
DCBAA,		0.037	0.111	
DBCAA, TBAA				
ClO_2^- , BrO_3^- ,	2D IC-CD	0.60, 0.35,	1.99, 1.20,	[217]
MCAA, MBAA,		0.30, 0.58,	1.01, 1.94,	
DCAA, DBAA,		0.34, 0.64, 0.46	1.13, 2.15,	
TCAA			1.54	
BrO_3^- , MCAA,	IC-ESI-	0.0051, 0.041,	<i>n.d.</i>	[248]
MBAA, MIAA,	MS/MS	0.014, 0.14,		
DCAA, BCAA,		0.010, 0.037,		
DBAA, CIAA,		0.44, 0.060,		
BIAA, DIAA,		0.024, 0.013,		
TCAA, BDCAA,		0.010, 0.030,		
CDBAA, TBAA		0.11, 0.10, 0.10		
BrO_3^- , ClO_3^- , Cl^- ,	IC-UV	2000, 2000,	<i>n.d.</i>	[58]
Br^-		5000, 5000		

n.d.: value not defined

More advanced IC approaches integrated gradient elution and MS for enhanced sensitivity. A seven-step gradient IC-CD method enabled detection of multiple analytes, including HAAs and halides, with LODs as low as $0.06 \mu\text{g L}^{-1}$ for chloride and $2.14 \mu\text{g L}^{-1}$ for bromide [140]. High-performance ion chromatography (HPIC), an advanced form of IC designed for high-resolution separation and improved detection limits, can be coupled with tandem mass spectrometry (MS/MS) to further enhance sensitivity [256]. Similarly, IC-ESI-MS can be employed, where ESI facilitates the transfer of analytes into the gas phase for MS detection, improving sensitivity for a broad range of halogenated species, with LODs spanning from 0.005 to $0.188 \mu\text{g L}^{-1}$ depending on the target compound [25,225,248]. Two-dimensional IC-CD (2D IC-CD), was used to improve separation efficiency by incorporating two chromatographic columns with different selectivity, however for bromate, chlorite, and HAAs the LOD results were not better than with tandem MS [217].

The presented works underscore the evolution of IC-based methodologies in terms of improving sensitivity and accuracy for the detection of halogenated contaminants in water samples. UV detector is not appropriate in this scenario, as shown by the very high values of LOD obtained by El Haddad et al. [58].

4.2.6. The relevance of MS detector in navigating DBP analysis

High-resolution mass spectrometry (HRMS), including time-of-flight, Orbitrap, and Fourier-transform instruments, has expanded DBP analysis beyond compounds available as authentic standards, because it provides accurate-mass full-scan and tandem mass spectra for suspect and nontarget screening. Suspect and nontarget screening of DBPs by HRMS generally relies on full-scan acquisition combined with either data-dependent acquisition (DDA) or data-independent acquisition (DIA). In DDA, precursor ions are selected from the full scan, usually

according to signal intensity, and subsequently fragmented. This approach often produces relatively clean MS/MS spectra, although low-abundance DBPs may not be selected. DIA acquires fragment-ion information over consecutive mass windows without preselecting individual precursor ions, thereby providing broader coverage of the detected chemical space. However, the resulting spectra are more complex, and the association of fragment ions with their corresponding precursors can be difficult in complex water extracts [43,261].

Post-acquisition processing typically includes blank subtraction, peak detection, molecular-formula assignment, isotope-pattern evaluation, halogen-specific screening, and interpretation of MS/MS spectra. Lu et al. [139] processed UPLC–HRMS data using Compound Discoverer for blank removal, peak picking, formula prediction, and fragment matching. Formula assignments were independently evaluated with the R package MFAssignR, after which a self-developed halogen extraction code was used to identify chlorine-containing features from the characteristic $^{35}\text{Cl}/^{37}\text{Cl}$ mass difference and isotope-abundance pattern. The combined workflow reduced false-positive assignments and supported the identification of 14 previously unreported Cl-DBPs formed from tyrosine and tryptophan. A related workflow was applied to chlorinated tannic acid, where MFAssignR provided molecular formulas, m/z values, peak intensities, and double-bond equivalent values, while the halogen extraction code isolated potential Cl-DBPs from the full dataset. Their structures were subsequently proposed from manual interpretation of MS/MS spectra and chemically plausible formation pathways, resulting in the identification of 17 novel Cl-DBPs [138].

Library-based screening has also been incorporated into commercial and custom data-processing platforms. Gao et al. [79] processed QTOF-MS^E data in UNIFI 1.9.3 using an in-house DBP library containing accurate mass, retention time, and structural information, together with a suspect library derived from the EPA CHLORINE_TPs database. Candidate features were filtered according to signal intensity, mass accuracy, retention-time agreement, and isotope-pattern matching. Low- and high-energy MS^E spectra were then examined to support the proposed assignments [79]. In a different approach, Fu et al. [73] developed the MATLAB-based NOMDBP code, an extension of the TRFu algorithm, for the simultaneous assignment of halogenated DBPs and nonhalogenated dissolved organic matter. Candidate formulas were screened using $^{35}\text{Cl}/^{37}\text{Cl}$ and $^{79}\text{Br}/^{81}\text{Br}$ isotope patterns and compared with a literature-derived X_n-DBP formula library. Additional filters were used to identify possible precursors and peaks appearing only after disinfection. The most plausible formulas were selected according to halogen content, oxygen content, nonoxygen heteroatom composition, and mass error, followed by reassignment of ^{37}Cl , ^{81}Br , ^{13}C , and ^{34}S isotopologues. Molecular descriptors and van Krevelen plots were subsequently used to examine DBP characteristics and possible formation pathways [73].

Structural assignments should be supported by several independent lines of evidence, including accurate mass, isotope distribution, diagnostic fragments, neutral losses, library matching, in silico fragmentation, retention behavior, and the plausibility of the proposed disinfection pathway [79,138]. Nevertheless, MS/MS data alone are often insufficient to distinguish positional isomers, particularly when authentic standards are unavailable. The position of halogen or functional-group substitution should therefore be regarded as tentative unless confirmed experimentally [138]. Identification confidence can be reported using the Schymanski framework, in which Level 1 denotes confirmation with an authentic standard, Level 2 a probable structure supported by library or diagnostic evidence, Level 3 one or more tentative structural candidates, Level 4 an unequivocal molecular formula, and Level 5 an accurate-mass feature without a unique formula assignment [203]. DBPs identified without reference standards should therefore be reported as probable or tentative rather than confirmed, even when accurate mass, isotope patterns, and MS/MS fragments support the proposed structure.

5. Regulation status and beyond

In December 2020, the adoption of the new Drinking Water Directive (DWD) included new legislative parameters concerning the monitoring of the DBPs [63]. This legislation entered into force in January 2021, modifying the directive created in 1998. The new directive was automatically transposed into the national law on 12 January 2023. The DWD is the main legislation in Europe for access to and the quality of water intended for human consumption. The main objectives of the directive are [51]:

- to protect human health by ensuring the quality of water intended for human consumption;
- to ensure that drinking water quality is controlled through standards based on the latest scientific evidence;
- to secure efficient and effective monitoring, assessment and enforcement of drinking water quality;
- to provide Europeans with adequate, timely and appropriately information;
- to improve access to water intended for human consumption.

5.1. Context of the revision of DWD

The recast is a response by the European Commission to the European Citizens' Initiative 'Right2Water', which advocated for access to drinking water for all [184]. This initiative was the main driver for the article on access to water in the new directive, in order to comply with Sustainable Development Goal 6. This revision of the directive was also linked to the microplastic pollution challenges in Europe.

During the political debates, the main discussion did not focus on the challenges related to the DBPs but rather on virus and microbiological aspects [62]. This perspective is also confirmed in the European Commission's Regulatory Fitness and Performance programme (REFIT) evaluation of the European Union (EU), which does not find *major incoherencies neither internally with Article 7(1) and its minimisation order for disinfection by-products, nor externally with Biocidal Products* [59].

The WHO was the major contributor to the reform of the DWD to include new DBPs-related parameters in the legislation. Indeed, the impact assessment and the study supporting the revision developed by the European Commission do not mention specifically the challenges of the DBPs. But the two reports include the necessity to review the list of monitoring parameters of the list A of the directive based on scientific and technical progress, referring to the WHO guidelines on the drinking water parameters [60,61].

In its guidelines, WHO stressed the limited perspective to monitor only THMs since they are not a good surrogate for all the DBPs.

5.2. The new elements on DBPs

The regulatory values/guidelines established by the EU, US EPA and WHO for the presence of HAAs, THMs and inorganic DBPs are compared in Table 7 – [57,183,245]. For the case of the THMs, while the US EPA sets a limit for all the individual THMs as well as their combination, WHO only presents guidelines for their presence individually and the EU their combined presence. For the THMs both individually and their total, the US EPA establishes stricter limits, among all these agencies. The European Institutions have followed the recommendations of the WHO with a more restrictive approach on the HAAs, reducing the limit to $60\ \mu\text{g L}^{-1}$, but limiting the monitoring of this group of DBPs only when the used disinfection methods can generate such types of DBPs. Both US EPA and the EU have established the limit for the total of five HAAs, including MCAA, DCAA, TCAA, MBAA and DBAA. Meanwhile WHO has only established guideline values for some individuals HAAs. Inorganic DBPs such as bromate, chlorite and chlorate are also subjected to limits with a disparity of control by these agencies. Bromate presents the same

limit in all the agencies, chlorite is regulated by US EPA and WHO, the latter presenting a stricter guideline value for this inorganic DBP. For chlorate, however, there is only the guideline presented by WHO. In comparison with the old DWD, the new one includes in its annex II part B, the mandatory monitoring of HAAs, along with the monitoring of THMs. The DBPs monitoring frequency is established in Table 1 of the new DWD, which depends on the volume of water distributed or produced each day within a supply zone. The two most extreme cases include a range of volume of water distributed or produced each day of ≥ 10 and $\leq 100 \text{ m}^3$, where the monitoring should be done once per year; and if it is $> 100000 \text{ m}^3$, the monitoring should be 12 samples per year for the first $10000 \text{ m}^3 \text{ d}^{-1}$ and an additional monitoring sample for each additional $25000 \text{ m}^3 \text{ d}^{-1}$. However, an increase in the monitoring frequency may be necessary if considered in the risk assessment plan of the supply system due to regional/local context [63].

5.3. Going beyond: ZeroPollution4Water cluster

As previously mentioned, the EU intends to look at the scientific and technical progress to recast its legislation. In this context, the research activities shall look at the implementation of this new DWD, including the identification of white spots. To achieve this, a collaboration between EU-funded research and innovation projects committed to protecting groundwater and drinking water was formed – the ZeroPollution4Water Cluster (ZP4WC).¹ In the scope of the ZP4WC, two joint policy briefs have already been released [269,270]. The first policy

Table 7 –

Parametric values for the regulated DBPs established by the New Drinking Water Directive of European Union and by the United States Environmental Protection Agency, and guidelines indicated by World Health Organization. These limits include both enforceable (*) and recommended (**) values. Retrieved from [57, 183,245].

Parameter		Entity		
		US EPA ($\mu\text{g L}^{-1}$)	WHO ($\mu\text{g L}^{-1}$)	EU ($\mu\text{g L}^{-1}$)
THMs	TCM	70 **	300	n.d.
	BDCM	0	60	n.d.
	CDBM	60 **	100	n.d.
	TBM	0	100	n.d.
	THMs total	80 *	n.d.	100 **
HAAs	MCAA	n.d.	20	n.d.
	DCAA	n.d.	50	n.d.
	TCAA	n.d.	200	n.d.
	MBAA	n.d.	n.d.	n.d.
	DBAA	n.d.	n.d.	n.d.
Inorganic DBPs	HAAs	60 *	n.d.	60 * ^b
	Bromate	10 *	10	10 *
	Chlorite	1000 *	700	n.d.
	Chlorate	n.d.	700	n.d.

^a Where possible, without compromising disinfection, Member States shall strive for a lower parametric value. It is the sum of concentrations of the following specified compounds: chloroform, bromoform, dibromochloromethane and bromodichloromethane.

^b This parameter shall be measured only when disinfection methods that can generate HAAs are used for the disinfection of water intended for human consumption. It is the sum of the following five representative substances: monochloro-, dichloro-, and trichloro-acetic acid, and mono- and dibromo-acetic acid.

¹ This cluster is an initiative originating from the coalition of seven different projects funded from two Horizon Europe 2022 calls which aim to prevent groundwater contamination and protect its quality against harmful impacts of global and climate change (1), and secure drinking water quality by protecting water sources against pollution, providing innovative monitoring and treatment solutions, and ensuring safe drinking water distribution (2). The founding projects were: NINFA, SafeCrew, Mar2Protect, H2OforAll, ToDrinQ, UPwater, intoDBP.

brief includes some conclusions from intoDBP (<https://cordis.europa.eu/project/id/101081728>) and H2OforAll (<https://cordis.europa.eu/project/id/101081963>) projects on the measure, methods and tools for control at source, a perspective on digital water, and gaps in research and innovation [269,270]. The second policy brief approaches DBPs, referring the importance of their study, strategies to reduce their formation, and how the New Drinking Water Directive is an opportunity to tackle DBP challenges [270].

Today, most DBPs are unregulated while the European Union is one of the main regulatory bodies on this topic. Particularly the I-DBPs should have more attention from the regulators. However, this current situation could be linked to the uncertainty on the specific NOM types yielding distinct DBPs. It requires further research activities to better understand this relationship to prevent the formation of DBPs and reduce the overall risks. The project intoDBP aimed to develop innovative and cost-effective sensors and analytical methods focused on DBPs to ensure water quality management. The project recommended a set of preventive and curative measures to tackle such pollution, giving a particular attention to the DBPs regulated by the new Drinking Water Directive and emerging ones [100]. The H2OforAll project aimed to develop cost-effective DBP sensor monitoring devices, models of contamination spreading, toxicity and environmental studies, proposed safeguarding measures for the drinking water chain and develop innovative water treatment methods to remove or prevent DBPs. Furthermore, it also aimed to create a central knowledge base with reliable data on DBPs in Europe and their effects [85]. The SafeCREW project aimed to develop a set of measures to monitor and reduce DBP precursors. In fact, it explored the characteristics of NOM and evaluated more precisely how different disinfection methods interact with this organic matter to generate these potentially harmful by-products [198]. The vision of the cluster is to tackle the water problems in a holistic way, thus other projects focused in different water sectors are being included and working together.

6. Future challenges

The recent DWD changes from European Union, while representing an important step forward in the regulation of DBPs, in fact shows a limited frame to the complexity of this problem. Despite aiming for more protection for public and environmental health, many DBPs remain unregulated, and concerns associated with non-chlorinated DBPs remain only superficially considered in policy discussions.

One major obstacle to overcome this is the uncertainty about how different types of NOM will contribute to the formation of DBPs, which is also linked to the water treatment methods. The composition of NOM is influenced by multiple factors, such as the source of the water, its environmental conditions and surrounding ecosystems. The lack of robust information results in inefficiencies in mitigating DBP formation and, consequently, in increased risks to public health and environmental impact. From now on, future research should therefore not only explore the characteristics of NOM but also evaluate more precisely how different disinfection methods interact with this organic matter to generate these potentially harmful by-products. This approach is urgent to develop proactive control and prevention strategies.

In addition, another concern is the obvious need for continuous review of DBPs monitoring parameters in each legislation, in line with the risk-based approach taken in the new DWD. The focus on measuring THMs as indicators of water quality is not only inappropriate but also potentially dangerous. WHO guidelines highlighted the importance of including other compounds, such as HAAs, which was conveniently addressed by the European Commission and US EPA. However, several obstacles do not allow the fast expansion of legislation to other DBP families, resulting in a reactive rather than preventive approach. One of these constraints is the lack of data regarding safety protocols to assess certain DBPs. Moreover, the experimental procedures of analytical techniques and their LOD and LOQ should be tailored and developed for

new DBP families, or, in alternative, non-target approaches should be explored linked to Artificial Intelligence capacities.

European research projects and clustering activities are important tools to improve our understanding of the emerging DBPs and to impact water management practices in a significant way. These scientific projects should lead to proposals of preventive and corrective measures that must be effectively implemented in a reasonable horizon. The development of innovative technologies for water treatment is not only desirable but should also be implemented in large scale to ensure the safety of drinking water in the future.

Finally, there should be a focus on the neglected DBPs when developing and integrating new monitoring technologies. Collaboration between universities, research centres, and regulatory agencies is crucial in this regard. DBP regulations and management strategies must be approached critically and with a strong commitment to research and innovation, in the context of a Planet under climate change stressors. In order to have effective guidelines and regulations, policy makers must stand for scientific data reporting the detection, monitoring, and mitigation of DBPs in drinking water. In this way, we could ensure water safety standards and availability for the upcoming generations.

CRediT authorship contribution statement

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Declaration of Competing Interest

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

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.jece.2026.124641](https://doi.org/10.1016/j.jece.2026.124641).

Data availability

Data will be made available on request.

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