Emerging disinfection byproducts: A review on their occurrence and control in drinking water treatment processes

Emerging disinfection byproducts: a review on their occurrence and control in drinking water treatment processes

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Abstract

The occurrence of disinfection byproducts (DBPs) is related both to drinking water treatment (DWT) processes and to raw water's characteristics. Emerging pollutants typically occur in low concentrations and are not removed by conventional DWT processes. Emerging DBPs appear within the DWT or in the distribution system due to the combination of disinfection agents (especially chlorine) with precursors as: natural organic matter (NOM), algal organic matter (AOM), anthropogenic contaminants (pesticides, pharmaceuticals, detergents etc.), brominated and iodinated compounds.

This study has as main goal a consistent analysis of the major problems caused by emerging DBPs to drinking water supplies. It presents a comprehensive review of the research efforts related to emerging DBPs considering three viewpoints: 1. an overview of their classification, legislative framework, methods of analysis, disinfection operational

conditions and removal processes; 2. their occurrence, fate, health effects and impacts; 3. the analysis of the advanced DWT processes that might be used for the removal and control of precursors and DBPs with a focus on pilot and full-scale installations. All presented case studies considered pollutants removed, process conditions and efficiencies, and a critical assessment of processes based on membranes, advanced oxidation and adsorption on activated carbon or other materials. The main challenges of the control and removal of emerging DBPs are their low concentrations and the technical and economic sustainability of the application at full-scale of the AOPs, which need to be carefully adapted to local boundary conditions.

Keywords: disinfection byproducts, emerging pollutants, drinking water, water treatment process

Contents

List of abbreviations

Abbreviations/ Chemical formulas	Complete name
ADWT	Advanced Drinking Water Treatment
AOM	Algal Organic Matter
AOPs	Advanced Oxidation Processes
BCAA	Bromochloroacetic acid
BDCAA	Bromodichloroacetic acid
BDCM	Bromodichloromethane
Br-DBPs	Brominated-Disinfection byproducts
C/F	Coagulation/Flocculation
C-DBPs	Carbonaceous disinfection byproducts
$CHCl_3$	Chloroform
Cl-DBPs	Chlorinated-Disinfection byproducts
DBAN	Dibromoacetonitrile
DBCM	Dibromochloromethane
DBPs	Disinfection byproducts
DCAA	Dichloroacetic acid
DCAcAm	2,2-dichloroacetamide
DCAN	Dichloroacetonitrile
DWT	Drinking Water Treatment
EDCs	Endocrine Disrupting Chemicals
EPs	Emerging pollutants
GAC	Granular Activated Carbon
GC-ECD	Gas Chromatography- Electron Capture Detector
GC-MS	Gas Chromatography- Mass Spectrometry
HAA5	Haloacetic Acids
HNM	Halonitromethane
HPLC	High-Performance Liquid Chromatography
HS-SPME	Solid-phase Microextraction in the Headspace
IC-MS/MS	Ion Chromatography-tandem Mass Spectrometry
I-DBPs	Iodinated disinfection byproducts
IER	Ion-exchange Resin
LLE-ETAC	Liquid-Liquid Extraction with Ethyl Acetate
MCAA	Monochloroacetic acid
MCL	Maximum Concentration Level
MLLE	Micro Liquid-Liquid Extraction
N-DBPs	Nitrogenous disinfection byproducts
NDMA	N-nitrosodimethylamine
NOM	Natural Organic Matter
PAC	Powdered Activated Carbon
PIE	Precursor Ion Elimination
TBAA	Tribromoacetic acid
TCAA	Trichloroacetic acid
TCAcAm	Trichloroacetamide
TCAN	Trichloroacetonitrile
TCNM	Trichloronitromethane
THM	Trihalomethane
TTHM	Total Trihalomethanes
UPLC	Ultra-Performance Liquid Chromatography

1. Introduction

A major accomplishment for human health is the production of safe drinking water from raw surface and ground waters. Drinking water sources have thus become a priority for environmental communities worldwide. Water disinfection plays a pivotal role in reducing serious illnesses associated with waterborne diseases. Disinfection is used to eliminate pathogenic microorganisms during the drinking water treatment (DWT) and to ensure in the distribution network the quality parameters for a safe drinking water consumption (Chau et al., 2015). DWT plants' managers and water suppliers must assume the responsibility for water safety and at the same time for the implementation of the most efficient technologies to warrant that all qualitative indicators are below the limits imposed by the regulations.

Most common chemical disinfectants are chlorine-based (e.g. chlorine, chlorine dioxide, hypochlorite salts), having the advantages of low cost and easy manipulation, high efficiency

65 towards different pathogens, taste improvement and persistence in the distribution network.
66 However, disinfection byproducts (DBPs) often occur after chlorine-based disinfection
67 processes (Gupta and Ali, 2013), implying possible adverse effects and risks to human
68 health. Many precursors, as natural organic matter (NOM), algal organic matter (AOM),
69 anthropogenic contaminants (e.g. pesticides, pharmaceuticals, detergents, etc.), brominated
70 and iodinated compounds, as well as upstream wastewater discharges, and DWT
71 operational parameters (disinfection agent type and/or dose, pH, contact time, temperature)
72 may contribute to the development of DBPs (Alexandrou et al., 2018). Precursors' presence
73 and amount could be subjected to seasonal variations (e.g. for AOM or contaminants related
74 to agricultural activities, as ammonium and pesticides). DBPs are classified "harmful for
75 human health" and their occurrence in raw water sources imposes special monitoring and
76 efforts for the water suppliers (WHO, 2017).
77 In order to avoid DBPs formation, new disinfection processes and technologies were
78 developed (e.g. ozone, ultraviolet, silver ion, electrochlorination, ferrate), involving high costs
79 related to equipment and energy consumption (Zainudin et al., 2018). However, DBPs
80 occurrence was demonstrated also for disinfection processes using non-chlorinated reagents
81 (Ding et al., 2019).
82 Many members of the drinking water protection community have been actively working to
83 clearly understand the possible negative effects of DBPs on human health. Meanwhile, state
84 and federal governments have taken steps to protect the public from the potential health
85 risks of DBPs by conducting research on their toxicological effects, strengthening drinking
86 water regulations and supporting improvements in water treatment technology (Bereskie et
87 al., 2017). Many authors focused their research on DBPs and disinfection processes under
88 the following directions: (i) occurrence and removal of DBPs precursors deriving from raw
89 water sources and optimization of DWT operational parameters and (ii) improved removal of
90 DBPs and residual microorganisms at the end of DWT process and within the distribution
91 network. Advanced drinking water treatment (ADWT) technologies are commonly

implemented for the removal of emerging pollutants (including DBPs) and to reduce the concentrations of organic/inorganic precursors (Teodosiu et al., 2018).

This study has as main goal a consistent analysis of the major problems caused by emerging DBPs to drinking water supplies, providing a foundation for future research and highlighting the strengths and weaknesses of DBPs' control processes. To our knowledge, most research focused so far on the identification of DBPs and their precursors rather than on removal technologies. This study has the aim to present a comprehensive review of the research efforts related to emerging DBPs considering three objectives: 1) an overview of their classification, legislative framework, methods of analysis, disinfection operational conditions and removal processes; 2) their occurrence, fate, health effects and impacts; 3) a critical assessment of the ADWT processes that might be used for the removal and control of emerging DBPs and their precursors with a specific focus on pilot and full-scale installations.

2. Methodology

The analysis of the scientific literature considered for this review was based on the following selection criteria:

- ✓ *The relevance of articles and international information databases*. This study was based on 202 documents: articles found in Science Direct, Scopus, Web of Science, Springer, Wiley Online Library, and reports downloaded from the European Commission or other international reference databases (162 scientific papers, 23 review papers, 17 books/technical reports/regulations);
- ✓ *Publication period*. The references are mostly from 2010-2020 (93.77 %);
- ✓ *Relevant keywords*. The following keywords have been used in different combinations: *drinking water treatment, disinfection, disinfection byproducts, treatment technologies, pilot scale, full scale, analysis of disinfection by products from drinking water, regulations*;

✓ *Selection of references based on content analysis*. On the grounds of the above-mentioned criteria, 202 references were finally analysed as abstracts or full text documents.

3. Emerging DBPs of concern for drinking water treatment processes

DBPs are formed in drinking water from the reaction of disinfection agents with other compounds (*precursors*) occurring in raw water as: NOM, bromide and iodide, anthropogenic compounds (pharmaceuticals, antibacterial agents, textile dyes, pesticides, surfactants and cyanotoxins, etc.) (Papageorgiou et al., 2016; Barcelo, 2012). In recent years, great efforts were made to study the fate, occurrence and ecotoxicology of byproducts of drinking water disinfection processes. During chlorination, a large number and variety of DBPs are formed (Bond et al., 2014), as trihalomethanes (THMs), haloacetic acids (HAAs), haloacetonitriles, halophenols and halopropanoles (Farré et al., 2008, Liu et al., 2017; Young et al., 2018). Some DBPs, like THMs, HAAs, chlorites and bromates, are acknowledged by USEPA, WHO and international regulations as they are considered to have high impacts on human health. However, other DBPs (Table 1) are unregulated, even if their presence was detected during disinfection (with chloramines, chlorine, chlorine dioxide, ozone or ferrate) or if raw water contains natural bromide (Jiang et al., 2016). Unregulated DBPs are less known and studied, having very low concentrations, but they can be more toxic for humans and can rapidly increase the risks for cancer or other diseases (Li et al., 2015).

3.1. Definition, classifications and regulations

Most DBPs could be defined *emerging pollutants* (EPs) (see Table 1), according to the Norman Network classification (Norman Network, 2016). EPs are chemical compounds with risks to human health, which appear in drinking water as a consequence of disinfection treatment (Table 1). Over 600 DBPs were identified (Richardson and Postigo, 2011), however the studies concerning their occurrence and formation mechanisms, human health

143 effects and treatment alternatives (Hebert et al., 2010; Kimura and Ortega-Hernandez, 2019;
144 Chaukura et al., 2020; Sorlini et al., 2014) are much less. Usually, DBPs are related to the
145 use of chlorine-based disinfectants (chlorine gas, chloramines, chlorine dioxide,
146 hypochlorite/hypochlorous acid) or ozone and to the raw water physicochemical features.
147 The most common DBPs classes, their sources and health effects are presented in Table 1.

148 **Table 1.** DBPs classes, sources and health effects

DBPs Classes	Recognized as EPs	Sources				Effects	References
		Cl	NH_2Cl	ClO_2	O_3		
Total Trihalomethanes (TTHMs or THM4)							
Bromodichloromethane	yes						
Bromoform							
Dibromochloromethane							
Chloroform		**x**	**x**	**x**		Possible carcinogenic for liver, kidney, intestine; central nervous and reproductive system diseases; also causing bladder, colon, rectal, or pancreatic cancer	Hebert et al., 2010; Pardakhti et al., 2011; Kogevinas et al., 2016; Lodhi et al., 2017; Han et al., 2017
Haloacetic acids (HAAs or HAA5)							
Dichloroacetic acid							
Trichloroacetic acid							
Chloroacetic acid	yes						
Bromoacetic acid							
Dibromoacetic acid		**x**	**x**			Possible carcinogenic for liver, kidney, lung, causing leukaemia; effects on reproductive system, skin and eyes irritation	Chowdhury et al., 2011; Dad et al., 2018
Bromate				**x**	**x**	Possible carcinogenic for thyroid, kidney and breast	Dongmei et al., 2015; Xiao et al., 2017
Chlorite				**x**		Anaemia, thyroid gland and kidney diseases; mutagenic and teratogenic effects on nervous system	Feretti et al., 2008; Garcia-Villanova et al., 2010; Chhetri et al., 2017
Chlorate	yes			**x**		Possible carcinogenic for thyroid; immune system hypersensitivity	Feretti et al., 2008; Hebert et al., 2010; Ibrahim and Abu-Shanab, 2013
Hydrazine	yes		**x**			Possible effects upon the nervous and cardiovascular system, liver and kidneys; causing vomiting and hepatotoxicity; carcinogenic and with chronic toxicity	Bond et al., 2011; Matsumoto et al., 2016; Guyton et al., 2018;

DBPs Classes	Recognized as EPs	Sources				Effects	References
		Cl	NH_2Cl	ClO_2	O_3		
Nitrosamines (NDMA) N-Nitrosodimethylamine N-Nitrosopyrrolidine N-Nitrosomorpholine N-Nitrosopiperidine N-Nitrosodiphenylamine N-nitrosomethylethylamine N-nitrosodiethylamine N-nitroso-di-n-butylamine	yes	**x**	**x**			Possible carcinogenic for liver, stomach, esophagus, bladder, lung, breast and brain	Hebert et al., 2010; Hanigan et al., 2017 Linge et al., 2017;
Aldehydes Chloroacetaldehyde Dichloroacetaldehyde Bromochloroacetaldehyde Tribromoacetaldehyde	yes	**x**		**x**	**x**	Possible carcinogenic for stomach and lung; reproductive system toxicity; causes depression and DNA damage	Hebert et al., 2010; Xie et al., 2016
Unregulated THMs Dibromomethane Bromochloromethane Tetrachloromethane Dibromodichloromethane	yes	**x**	**x**			Possible carcinogenic for liver, kidney, intestine; central nervous and reproductive systems diseases;	Hebert et al., 2010 Yang et al., 2019
Unregulated HAAs Bromochloroacetic acid Bromodichloroacetic acid Dibromochloroacetic acid Tribromoacetic acid	yes	**x**	**x**			Possible carcinogenic for liver, lungs, kidney and reproductive system diseases; leukemia	Richardson et al., 2007; Hebert et al., 2010; Zhang et al., 2011
Tribromopyrrole/ Halopyrole	yes	**x**	**x**	**x**	**x**	Possible carcinogenic for breast	Hebert et al., 2010; Yang and Zhang, 2014
Cyanogen chloride	yes	**x**	**x**		**x**	Possibly causes eyes and skin irritation, respiratory and cardiovascular deficiencies; may be lethal at high concentration	Hebert et al., 2010; Weng and Blatchley, 2013;
Haloanisoles 2,4,6-trichloroanisol 2,4,6-tribromoanisole 2,4-dibromoanisole 2,4-dichloroanisole 2,6-dichloroanisole 2-bromoanisole 4-bromoanisole	yes	**x**				N/A	Hebert et al., 2010; Barceló and Alastuey, 2012; Xie et al., 2016
Chlorophenols 2-chlorophenol 2,4-Dichlorophenol 2,4,6-Trichlorophenol 2,3,4,6-Tetrachlorophenol 2,4,5-Trichlorophenol 4-chlorophenol	yes	**x**	**x**			Possible carcinogenic for liver, lymphoma and lungs; immune system hypersensitivity; hepatic and renal toxicity	Gopal et al., 2007; Hebert et al., 2010; Igbinosa et al., 2013; Zhai et al., 2014
Haloamides Dichloroacetamide Bromochloroacetamide Dibromoacetamide Bromoiodoacetamide Trichloroacetamide Diiodoacetamide Tribromoacetamide	yes	**x**	**x**			Possible carcinogenic effects on reproductive system, liver or leukemia	Hebert et al., 2010; Bull et al., 2011; Shah et al., 2012

DBPs Classes	Recognized as EPs	Sources				Effects	References
		Cl	NH_2Cl	ClO_2	O_3		
Halonitromethanes Chloronitromethane Bromonitromethane Dichloronitromethane Dibromonitromethane Bromochloronitromethane Trichloronitromethane Dibromochloronitromethane Tribromonitromethane	yes	**x**	**x**	**x**	**x**	Possible carcinogenic for breast	Liviac et al., 2009; Hebert et al., 2010; Ceretti et al., 2016;
Haloacetonitriles (HANs) Chloroacetonitrile Bromoacetonitrile Dichloroacetonitrile Bromochloroacetonitrile Trichloroacetonitrile Iodoacetonitrile Dibromoacetonitrile	yes	**x**	**x**	**x**	**x**	Reproductive system toxicity; possible carcinogenic for breast	Richardson et al., 2007; Hebert et al., 2010; Ileka-Priouzeau et al., 2015;
Haloketones Hexachloropropanone 1,1-Dibromopropanone 1,1,3-Trichloropropanone 1,1,1,3-Tetrachloropropanone 1,1,3,3 Tetrachloropropanone 1,1,1,3,3Pentachloropropanone	yes	**x**	**x**			Possible carcinogenic or mutagenic effects	Hebert et al., 2010; Linge et al., 2013; Zhai et al., 2014
Iodoacids	yes		**x**			Possible cytotoxic and genotoxic effects, causing breast cancer	Hebert et al., 2010; Xiao et al., 2016
IodoTHMs Dichloroiodomethane Bromochloroiodomethane Bromodiiodomethane Dibromoiodomethane Chlorodiiodomethane Iodoform	yes	**x**	**x**	**x**		Possible genotoxic and cytotoxic effects, causing bleeder cancer and endocrine diseases	Hebert et al., 2010; Luo et al., 2014; Han et al., 2017
HEX & TEX Hexachlorocyclopentadiene Tetrachlorocyclopentadiene	yes		**x**			Possible carcinogenic for liver, causing skin and eyes irritation	Hebert et al., 2010; TOXNET, 2018
MX & halofuranones Mutagen X Mucochloric acid	yes	**x**	**x**	**x**		Possible carcinogenic for thyroid, bile duct, pancreas and lungs	Hebert et al., 2010; Richardson and Postigo, 2016

Note: N/A – not applicable/not available

Apart of the identification of DBPs and their adverse health effects, international regulations and guidelines also defined maximum amounts of DBPs allowed in drinking water. The World Health Organization (WHO) introduced Drinking Water Guidelines with maximum contaminant levels for DBPs (WHO, 2006; WHO, 2008; WHO, 2017). The Environmental Protection Agency (USEPA, 2009) regulates DBPs like THMs, HAAs, bromate and chlorite. USEPA specifically regulates five HAAs, defined HAA5 (Table 1). In Europe, only THM4

(Table 1) and bromate are regulated as DBPs through the Drinking Water Directive, but there are standards and guidelines for each species of THMs (Karanfil et al., 2008). Wang et al. (2015) compared the maximum contaminant levels (MCL, expressed as μg L^{-1}) for regulated DBPs in drinking water according to international regulations and guidelines (Table 2). However, MCL values do not characterize DBPs from the point of view of toxicity, carcinogenicity and occurrence (Hebert et al., 2010).

Table 2. Maximum contaminant levels for DBPs as in current directives and guidelines (adapted from Wang et al., 2015)

DBPs	**MCL (μg L^{-1})**							
	WHO guidelines (a)	USA Guidelines (b)	Canadian Guidelines (c)	Australian guidelines (d)	EU Directive (e)	Japanese standards (f)	Chinese regulations (g)	Egyptian standards (k)
TTHM(h)	**1000**	**80**	**100** LRAA(i)	**250**	**100**	**100**	**1000**	**100**
Cloroform(l)	**300**	-	-	-	-	**60**	**60**	**1000**
BDCM (n)	**60**	-	**16**	-	-	**30**	**60**	**500**
DBCM (n)	**100**	-	-	-	-	**100**	**100**	**500**
Bromoform (l,n)	**100**	80	-	-	-	**90**	**100**	**200**
HAA5(j)	**60**	**60**	**80** LRAA	-	-	**-**	-	-
MCAA	20	-	-	**150**	-	**20**	-	-
DCAA	50	-	-	**100**	-	**30**	**50**	
DCAN(k)	20	-	-	N.D.	-	**-**	-	**1000**
DBAN	70	-	-	N.D.	-	**-**	-	**1000**
TCAA	200	-	-	**100**	-	**30**	**100**	**-**
TCAN	-	-	-	-	-	**-**	-	**100**
CH (k)	-	-	-	**100**	-	**-**	**10**	**200**
Bromate (l,p)	10	**10**	**10**	20	**10**	**10**	**10**	-
Formaldehyde	-	-	-	**500**	-	**80**	**900**	-
Chlorite (l,m)	700	**1000**	**1000**	800	-	**-**	**700**	-
Chlorate (m)	700	700	**1000**	N.D.	-		**700**	-
CHCl (as CN) (l)	-	-	-	80	-	**10**	**70**	-
2-chlorophenol (o)	-	-	-	**300**	-	-	-	-
2,4-dichlorophenol (o)	-	-	**900**	**200**	-	-	-	-
2,4,6-dichlorophenol (o)	200	-	2	**20**	-	-	**200**	-
2,3,4,6-Tetrachlorophenol(o)	-	-	**100**	-	-	-	-	-
NDMA (nitrosamines)	0.1	-	**0.04**	0.1	-	-	-	-
Chloropicrin (q)	-	-	**-**	-	-	-	-	**500**
1,1,1-Trichloropropane (q)	-	-	**-**	-	-	-	-	**500**

Notes and abbreviations: (a) World Health Organization guidelines – (*WHO*, 2017); (b) United States of America guidelines– (*US EPA*, 2006); (c) Canadian Guidelines 2019 - (*Canadian DWQ*, 2019); (d) Australian guidelines – (*NWQMS*, 2016); (e) Drinking Water Directive of European Council 2012 - (*Directive 98/83/EC*, 1998); (f) Ministry of Health, Labour and Welfare (*Japanese Standards*, 2016, *JWWA*, 2016); (g) Chinese regulation (*GB 5749-2006*, 2007); (h) TTHM - Sum of all THMs contaminants; (i) LRAA - Local Running Annual Average; (j) HAA5 - Haloacetic Acids (k) Ibrahim and Abu-Shanab, 2013; (l) Richardson, 2005; (m) Al-Otoum *et al.*, 2016; (n) Pérez Pavón *et al.*, 2008; (o) Hebert *et al.*, 2010; (p) Winid, 2015; (q) Ali, 2013

Explanation: Values in bold refer to DBPs included in the international guidelines, regulations, standards and directives specified in brackets from point (a) to (g) and (k). Notes in brackets as (h), (i) and (j) are abbreviations explained. The rest are references for DBPs not included in the international regulations/guidelines.

3.2. DBPs sources and occurrence

To state the importance of the disinfection processes in providing safe drinking water for human consumption, the disinfectants used, with their main characteristics and effectiveness should be considered, along with the byproducts formed and consequent health risks. Figure 1 presents the sources and technologies that may remove both precursors and already formed-DBPs, these technologies being largely influenced by the outline of the DWT process scheme and of the distribution system.

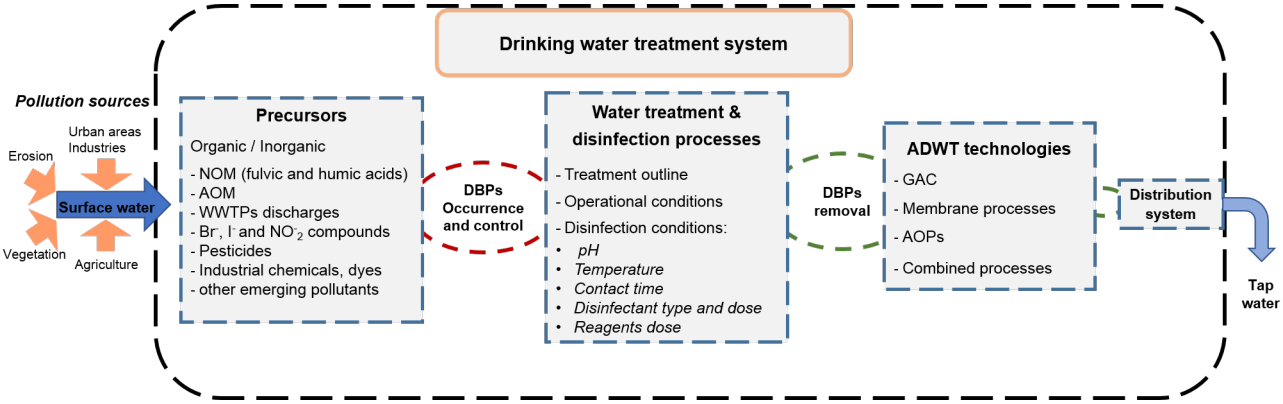

Fig. 1. Disinfection byproducts in a DWT system – from occurrence to removal.

DBPs formation mechanisms are strongly influenced by operational parameters such as: type of disinfectant used, dose and contact time, and by the physico-chemical features of raw water (pH, temperature, NOM, ammonium, metals) (Shahi et al., 2019; Jiang et al., 2018; Gougoutsa et al., 2016; Ibrahim and Abu-Shanab, 2013; Wei et al., 2010). Raw water characteristics are crucial, and many substances were identified as DBPs precursors: NOM (Sillanpää, 2014; Neale et al., 2019), pharmaceuticals (Ternes and von Gunten, 2010; Zhou et al., 2016), antibacterial agents (Barceló, 2012), textile dyes (Alves de Lima et al., 2007), pesticides (Duirk and Collette, 2006; Mehrsheikh et al., 2006), bisphenol A (Hu et al., 2002), alkylphenol ethoxylate surfactants (Petrovic et al., 2010) and cyanotoxins (Lee et al., 2017; Corbe et al., 2014). It is more effective to remove DBPs precursors before disinfection or to control its operational parameters than removing the already formed DBPs (Lin et al., 2016). NOM (especially humic substances), AOM, bromide, iodide and anthropogenic pollutants

have been widely investigated in raw water sources as precursors (López-Roldán et al., 2016; Chaukura et al., 2020).

Water sources are often affected by industrial discharges, agriculture runoffs, algal blooms, municipal wastewater discharges, storm water runoffs, wildfires and elevated bromine and iodine concentration, each with high or moderate impact on DBPs occurrence (Sgroi et al., 2018). Pharmaceuticals reach drinking water due to inadequate wastewater treatment, exaggerated human consumption and veterinary use, even through leaks from the agricultural lands. Even if they are present in low concentrations, pharmaceuticals can resist conventional DWT (e.g. flocculation, sedimentation, filtration) and chemical disinfection (through chlorine, chloramines, ozone or chlorine dioxide) (Kaplan, 2013) and produce DBPs (Postigo and Richardson, 2014; Kimura and Ortega-Hernandez, 2019). Advanced DWT systems that use UV or UV/H_2O_2 disinfection processes can interact with pharmaceutical substances and form NDMA or increased levels of DBPs after the addition of chloramine (Radjenovic et al., 2012; Postigo and Richardson, 2014).

Disinfectants like chlorine, chlorine dioxide, chloramine, sodium hypochloride or ozone interact with NOM, microorganisms or bromide/iodide to produce a different class of DBPs with a high toxicity (Zhao et al., 2012; Jiang et al., 2018).

In the following subsections an overview of the main disinfection agents used in DWT processes and the generated DBPs will be presented.

3.2.1. Chlorine

Within chlorine disinfection, TCAA and DCAA are the major DBPs formed, followed by THMs (Zhai et al., 2017; Di Cristo et al., 2015). NOM presence in raw water has a high potential to generate THMs and HAAs during the chlorination process and it is correlated with seasonal variations and water quality parameters (Alver et al., 2018). AOM is a precursor as well and during chlorination leads to C-DBPs and N-DBPs (Qi et al., 2016; Goslan et al., 2017), depending both on AOM concentration and on the chlorine dose and contact time.

228 Coagulation/flocculation process is essential to achieve high NOM and AOM removal
229 efficiencies, while a well-adjusted coagulant dose influences the performances of suspended
230 solids removal (Gad-Allah et al., 2012; Zaleschi et al., 2012). Recent studies indicated that
231 chlorine might attack NOM and form intermediate DBPs (including nonhalogenated and
232 halogenated aromatic DBPs) (Jiang et al., 2017), and finally form halogenated aliphatic
233 DBPs (including regulated THMs and HAAs) (Jiang et al., 2020, Li et al., 2020). Similarly,
234 nitrogenous DBPs formed during chlorination depend on disinfectant dose and pH (5 to 6),
235 while the high temperature increases the formation potential of TCNM (Chen et al., 2017).
236 A study involving water disinfection with chlorine, UV, UV/chlorine and UV/H_2O_2 (Wang et al.,
237 2015), showed that DBPs formation during UV/chlorine AOPs depended on chlorine dose,
238 exposure time and quality of water sources. The formation of THM and HAA during
239 disinfection was low and constant for the three types of disinfection processes and depended
240 on pH, temperature and season.
241 Chlorine used as disinfection agent in special conditions (seasonal variation, temperature,
242 dose or drinking water quality) can form Haloacetamides (Kimura et al., 2019) or
243 Dimethylamine (de Vera et al., 2017). The formation of $CHCl_3$ or N-DBPs during UV/chlorine
244 disinfection occurred, as demonstrated by a study of Kimura et al. (2019). HAAs as TCAA,
245 hydroquinone, DCAA presented a high formation potential during chlorination under short-
246 term and long-term contact time conditions (Cordero et al.,2020). N-nitrosodimethylamine
247 formation occurred when chlorination was applied to a surface DWT plant (Orak et al., 2019).
248 Also, dichloroacetonitrile (DCAN) and dichloroacetamide (DCAcAm) occurred after the
249 chlorination process (Chen et al., 2019). AOM is a major precursor of halogenated
250 carbonaceous and nitrogenous byproducts (C-DBPs and N-DBPs) in the chlorination
251 process (Wu et al., 2020; Maeng et al., 2019).

252 3.2.2. Chlorine dioxide

253 The increased application of chlorine dioxide in DWT, particularly for surface water, avoids
254 the formation of THMs but can generate other DBPs: chlorite and chlorate, both supposed to
255 act as endocrine disruptors affecting human thyroid (Snyder et al., 2009). Chlorite (ClO_2^-)
256 and chlorate (ClO_3^-) are well-known degradation products of hypochlorite solutions.
257 Hypochlorite ion (OCl^-) is unstable and naturally undergoes two independent paths of self-
258 decomposition: one generating oxygen and chloride (Eq. 1), and the other chlorate and
259 chloride ions (Eq. 2):

260 $$2OCl^- \rightarrow O_2 + 2\ Cl^- \qquad \text{(Eq. 1)}$$

261 $$3OCl^- \rightarrow ClO_3^- + 2\ Cl^- \qquad \text{(Eq. 2)}$$

262 Chlorite is rapidly formed as an intermediate between hypochlorite and chlorate in (Eq. 2)
263 (Snyder et al., 2009). Chlorine dioxide (ClO_2), in contact with organic and inorganic
264 oxidizable substances (DBPs precursors), degrades to chlorite, chlorate and chloride ions,
265 thus reducing the subsequent possibility of THMs and HAAs developing in the distribution
266 networks (Al-Otoum et al., 2016; Ye et al., 2019). Chlorite levels may vary between 10-20 %
267 of ClO_2 dose in winter and 40-70 % in summer, while chlorate levels usually are between 10
268 and 30 % of the ClO_2 dose (Gates et al., 2009). Chlorine dioxide, in the presence of
269 hypochlorite, may undergo a disproportionation reaction to form chlorate (Eq. 3) (Gates et
270 al., 2009):

271 $$2ClO_2 + HClO + H_2O \Leftrightarrow 2ClO_3^- + Cl^- + 3H^+ \qquad \text{(Eq. 3)}$$

272 The factors commonly assumed to be of main influence in chlorite and chlorate generation
273 are: temperature and sunlight, which may catalyze the reactions presented in Eqs. 1- 3;
274 hypochlorite and chlorine dioxide doses; characteristics of raw water, particularly the
275 presence of transition metals and other oxidizable substances (Gates et al., 2009; Snyder et
276 al., 2009; Garcia-Villanova et al., 2010). It was found that DBPs occurrence during sodium
277 hypochlorite disinfection was affected by bromide ions (Rong et al., 2018).
278 DBPs formation (anhydroerythromycin, N-desmethyl clarithromycin and N-desmethyl
279 clarithromycin), occurred after chlorine dioxide treatment in the raw water of a DWT plant

280 located in Barcelona. Anhydroerythromycin was removed by both conventional (ozonisation)
281 and advanced (reverse osmosis) processes, and N-desmethyl clarithromycin was removed
282 only after ADWT (Rubirola et al., 2019).

283 3.2.3. Chloramination

284 NOM is considered the main precursor of DBPs, it is usually associated with surface waters
285 and interacts with chloramine forming THMs, HAAs and HANs. Dissolved fractions of organic
286 nitrogen and carbon (DON and DOC) play an essential role in the formation of C-DBPs and
287 N-DBPs in the pre-chloramination stage during summer (Chu et al., 2011). NOM with higher
288 aromaticity in the reaction with chloramine increased phenolic I-DBPs and decreased polar
289 aliphatic I-DBPs (Pan et al., 2016).
290 I-DBPs formation in the presence of zero-valent iron (ZVI) during chloramination is strongly
291 influenced by the same operational parameters (initial pH, IO_3 concentrations and
292 disinfectant dose). However, ZVI presence, iron corrosion scale, phosphate concentration
293 and Br-/IO3- molar ratio accelerated the formation potential of I-THMs (Xia et al., 2017).
294 THMs and HAAs are the most abundant DBPs generated by hypochlorite, while HANs may
295 derive from chloramines.
296 ADWT systems that use UV or UV/H_2O_2 disinfection processes can interact with
297 pharmaceutical substances and form NDMA or increased concentrations of DBPs after the
298 addition of chloramine (Radjenovic et al., 2012; Postigo and Richardson, 2014). During the
299 chloramination process used for DWT some DBPs are formed, especially Nitrosamines
300 (Selles et al., 2018), N-DBPs and Chloroform (Kimura et al., 2019) or NDMA (Ding et al.,
301 2019). Chloramine disinfection reagent contribute to the formation of NDMA and THMs,
302 respectively, both of which are defined as disinfection byproducts (Orak et al., 2019). Iodo-
303 THMs (DCIM, DBIM, BCIM, CDIM and TIM) occurred in 65 water treatment systems in
304 Canada during drinking water disinfection process with chloramine, and their concentration
305 ranged from 0.02 μg/L to 21.66 μg/L, due to various water quality parameters, seasonal

306 variations and relevant precursors content (DOC, bromide, iodide and iodine) (Tugulea et al.,
307 2018).

308 3.2.4. Ozone

309 When ozonation is followed by chlorination, the concentration of brominated and iodinated
310 THMs and HAAs increases, but nitrosamines formation is inhibited at high concentrations of
311 bromide (Zha et al., 2014). It was reported that in surface waters, bromides converted to
312 brominated DBPs has a potential hazardous impact on living organisms, especially on the
313 endocrine system, and on the aquatic environment (Watson et al., 2015; Winid, 2015).
314 In the presence of chlorine, chloramine or ozone, bromide and iodide halogenated ions
315 influence the amount of Cl-DBPs, Br-DBPs or I-DBPs and not only THMs, HAAs and N-
316 nitrosodimethylamine (Pan et al., 2015). Iodide compounds form hypoiodous acid/iodine by
317 disinfection processes with chlorine, monochloramine and ozone, or iodine-radicals by
318 chlorine dioxide. Bromate formation can be inhibited during water treatment process by
319 adapting ozonation to electro-peroxone process by a carbon-based cathode and production
320 of H_2O_2 from O_2. In this case, Br-DBP is reduced, while NOM removal in the drinking water
321 treatment process increases (Li et al., 2015).
322 Carboxylic acids may occur after disinfection, especially when chlorine and ozone are used
323 (Richardson et al., 2000), their amount varying due to raw water quality and DWT processes.
324 Jurado-Sánchez et al. (2014) detected 35 aliphatic and aromatic acids in two DWT plants
325 characterized by different process outlines. The first plant used chlorination/ chloramination
326 while the second one used ozonation and chlorination; the presence of the carboxylic acids
327 being 6 times higher in the second plant, the number of generated carboxylic acids
328 increasing especially in autumn and winter seasons. NDMA (Kimura et al., 2019) and
329 Hydroxylamine (Heeb et al., 2017) are some DBPs formed during drinking water disinfection
330 with ozone especially under various conditions (ozone dosages, pH) and different

components in water (bromide ion (Br^-), bicarbonate ion (HCO_3^-), sulfate ion (SO_4^{2-}), and humic acid (HA), as well as NOM from a lake (Shen et al., 2019).

3.2.5. Ferrate

A new disinfection agent is ferrate (Fe IV), which can successfully be applied on DWT processes given its oxidation, coagulation (Prucek et al., 2013) and disinfection (Alsheyab et al., 2009) abilities. It also limits DBPs generation and contributes to NOM and EPs elimination (Jiang, 2013). DBPs formation through chlorine dioxide or ferrate used for surface water treatment show that the production of THM, haloketones, haloacetonitriles and trichloronitromethane is higher for chlorine dioxide (Yang et al., 2013, Liu et al., 2020). Few studies regarding DBPs formation reported that high doses of ferrate (21 mg/L) can reduce nitrosamines up to 84 % (Lee et al., 2008) or react with amino acids, resulting in aldehydes (Sharma, 2010). Halogenated DBPs (including THMs, HAAs, haloketones, chloral hydrate, haloacetonitriles and trichloronitromethane) are the byproducts resulted from the disinfection of water with ferrate in presence of an important precursor such as AOM (Dong et al., 2019).

3.2.6. Multi stage disinfection processes and the influence of the distribution system

Other crucial issues about DBPs generation refer to the type and dose of disinfectants, related to raw water quality and size of DWT plant. While in small DWT plants, particularly those dedicated to groundwater treatment, a single-phase disinfection is usually adopted, large DWT plants generally perform multi-stage disinfection processes. In such systems, primary disinfection targets the removal of pollutants and pathogens (usually by means of ozone or chlorine dioxide). While secondary disinfection has the main goal of assuring drinking water quality along the water distribution network up to the final users. As a result, primary and secondary disinfectants are both considered DBPs' potential sources and their interaction should be taken into account. Hypochlorite is usually employed as secondary disinfectant because of its persistence in the distribution network, therefore most

international regulations call for a residual chlorine concentration in drinking water (e.g. EU requires 0.2 mg/L through Directive 98/83/CE) (EC, 1998). Another relevant factor that can influence DBPs formation is the seasonal variation of the surface water characteristics. Higher temperature determines the use of an increased dose of disinfectant (aimed to control the increase in pathogens growth) and supports its reaction with NOM, leading to high DBPs formation in summer and autumn (Ibrahim and Abu-Shanab, 2013; Guilherme and Rodriguez, 2014), while HAAs concentration is higher in the cold season (Wei et al., 2010). The occurrence of DBPs in the drinking water network is variable, and their concentration range does not depend on the size of the network itself (Guilherme and Rodriguez, 2015). At the same time, DBPs concentration can fluctuate within the DWT, so the difficulty of their removal consists in choosing an appropriate process outline, taking into account: spatial location of the treatment system, raw water extraction quality, seasonal and short-term variations (Mercier-Shanks, et al., 2013). The fluctuating levels of THMs and HAAs across the treatment system show a temporal and spatial variability of their concentrations, which hinders the monitoring process and makes it difficult to choose a period or point of sampling (Guilherme and Rodriguez, 2015). Recent studies emphasized the role of different chemical agents and treatment/piping materials of the DWT or distribution system on DBPs formation. Besides additional DBPs precursors (phenolic structures, amino acids, oligopeptides and nitrogen-containing contaminants), another concern is that certain treatment stages have the potential to transform DBPs into more toxic compounds. For example, activated carbon, ion-exchange resins or membrane treatments can increase the ratios of Br-DBPs to Cl-DBPs, resulting in higher mammalian cell cytotoxicity and genotoxicity, although the overall DBPs concentrations decrease (Ding et al., 2019). Also, in the distribution systems the main challenges include the maintenance of stable concentrations of residual disinfectant and the control of microbial content that may form DBPs as consequence of residual decay processes. Microbial activity is a complex process and many factors (temperature, water age, piping material, corrosion products,

384 nutrients, natural organic matter, hydraulic condition and disinfectant residual type and
385 dosage) could influence it. Disinfectant types and dose were found to be among the most
386 important factors driving the occurrence of DBPs in distribution networks (Li et al., 2019).
387
388 *3.3. Methods of analysis*
389 Most common methods for DBPs analysis include (Table 3): LC/ESI-MS/MS (liquid
390 chromatography-electrospray ionization tandem mass spectrometry) for determination of
391 chlorinated and brominated DBPs (Nollet and De Gelder, 2014) and also used to detect
392 polar halogenated DBPs, especially aromatic DBPs (Yang et al., 2019); capillary
393 electrophoresis (CE) (Kubáň et al., 2012) and high-field asymmetric waveform ion mobility
394 spectrometry (FAIMS-MS) for HAA analysis (Barceló et al., 2012); membrane-introduction
395 mass spectrometry (MIMS) for CNX (cyanogen halide) (Barceló et al., 2012); FT-ICR MS
396 (Fourier transform ion cyclotron resonance mass spectrometry) for bromate and brominated
397 DBPs (Yang and Zhang, 2016); SPE-LC-MS/MS (solid phase extraction-liquid
398 chromatography-tandem mass spectrometry) for haloquinones investigation from WTPs (Li
399 et al., 2011). Gas chromatography coupled with Orbitrap-based on mass spectrometry was
400 used for I-DBPs analysis (Cojocariu et al., 2016), GC-ECD was reported to identify the DBPs
401 formed by UV/chlorine disinfection (Huang et al., 2017) and GC-MS was able to detect
402 specific DBPs with low molecular weight (Yang and Zhang, 2016). Other specific analytical
403 methods for emerging DBPs detection include: High-Resolution Mass Spectrometry (HR-
404 MS) (Richardson and Postigo, 2016); Ion Chromatography-Mass Spectrometry (Bruzzoniti et
405 al., 2019), combined SPE, DCLCHR-LCMS and PIE (Zulkifli et al., 2018). HNMs HANs,
406 HAcAms, NDMAs and other emerging N-DBPs (Ding and Chu, 2017) are commonly
407 analyzed using GC (Pozzi et al., 2011; Chen et al., 2015; Ma et al., 2014; Montesinos and
408 Gallego, 2012), HPLC (Chu et al., 2012; Kodamatani et al., 2016) and UPLC (Müller et al.,
409 2012; Ripollés et al., 2011).
410

411 **Table 3.** Analytical techniques used for DBPs measurement

Analysis method	DBPs analyzed	Reference
SPE-HPLC-MS/MS	I-HAAs and aromatic I-DBPs	Hu et al., 2018
FT-ICR MS	Br-DBP	Yang and Zhang, 2016
GC-O/MS	I-DBP	Cojocariu et al., 2016
GC MS	HNMs HANs, HAcAms, NDMAs and emerging N-DBPs	Ding and Chu, 2017; Pozzi et al., 2011; Chen et al., 2015; Ma et al., 2014; Montesinos and Gallego, 2012
HPLC MS		Chu et al., 2012; Kodamatani et al., 2016
UPLC		Müller et al., 2012; Ripollés et al., 2011
LC/ESI-MS/MS	Chlorinated and Brominated DBPs	Nollet and De Gelder, 2014
	halogenated DBPs	Yang et al., 2019
MIMS	CNX HAA	Barceló et al., 2012
CE		
FAIMS-MS		
HPLC-MS	Hydrazine	Susinskis et al., 2018
IC-MS/MS	Nine HAAs, bromate, dalapon and I-HAAs	Wu et al., 2017
UHPLC/QTOF-MS	NDMA	Hanigan et al., 2017
GS-ECD	THMs, THAs, HANs and HKs	Huang et al., 2017
LLE-ETAC	DCAcAm	Lin et al., 2016
HS-SPME/GC-MS	Haloketones	Serrano, M., et al., 2015
LC/HR-MS	N-DBPs	Kolkman et al., 2015
MLLE	Haloketones	Serrano, M., et al., 2014
UPLC/ESI–MS–MS	Halobenzoquinones (HBQs)	Huang et al., 2013
SPE-LC-MS/MS	Haloquinones	Li et al., 2011

412

413 *3.4. Environmental and health impacts*

414 Human organisms can be exposed to DBPs through three conventional pathways: dermal
415 contact, ingestion or inhalation (Nieuwenhuijsen et al., 2009; Chowdhury et al., 2011;
416 Chaves et al. 2019; Chowdhury et al., 2020; Gonsioroski et al. 2020). The presence of DBPs
417 in drinking water became a human health concern because some epidemiological studies
418 demonstrated associations between DBPs exposure and increased risk of cancer
419 development, liver, kidney defects and central nervous system problems, adverse
420 reproductive outcomes (Legay et al., 2010; Chowdhury et al., 2017; Chen et al., 2019; Wang
421 et al.,2019; Gonsioroski et al., 2020) and endocrine disruption (Chaves et al., 2020). Urinary
422 bladder cancer has been the health risk most consistently associated with chlorination DBPs

(Hrudey et al., 2015; Regli et al.,2015; Chaves et al. 2019; Diana et al., 2019). Another study (Jones et al., 2019) evaluated the association between high DBPs levels with increased risk of colon and rectal cancer, however positive associations with individual THMs and HAAs, most consistent for rectal cancer, require further investigations.

Emerging DBPs formed in distribution system during chlorination and chloramination (THMs, HAA and HANs) have been reported to cause symptoms such as liver, kidneys and nervous system diseases and health risks associated with these regulated DBPs can be spontaneous abortions, births defects, stillbirths and negative reproductive effects (Quintiliani et al., 2018). Recent research focused on maternal exposure to emerging DBPs (THMs and TCAA) during pregnancy, and some DNA anomalies were observed in cord blood (Yang et al., 2017; Salas et al., 2015) causing foetal growth restriction (Cao et al., 2016) or other adverse reproductive outcomes (Wang et al., 2016; Holmes et al., 2017). Rivera-Nunez et al. evaluated the association between maternal exposure to THMs and DCAA. In a study of 2460 cases in Massachusetts from 1997 to 2004, chloroform, BDCM (Lodhi et al., 2017) and DCAA exposures (Dad et al., 2018) were associated with stillbirths (Rivera-Nunez et al., 2018). In a study of 7438 singleton term babies in United Kingdom, THMs and HAA% exposure during pregnancy was associated with reduced birth weight, but suggested differences by ethnicity (Smith et al., 2016). Halomethanes, iodo-trihalomethanes, nitrosamines, halobenzoquinones, NDMA, DCAN, DBAN exposure has been shown to be more genotoxic and cytotoxic than some regulated compounds, reinforcing their potential toxicological effect to humans (Chaves et al., 2020), and posing higher cancer risks for children than for adults (Luo et al., 2020).

Emerging DBPs may be classified as carcinogenic substances (Di Cristo et al., 2015; Ng et al., 2016) or may affect human health due to effects like: alteration of pregnancy duration, menstrual cycle or pregnancy loss, foetal development and congenital malformations or cancer (Villanueva et al., 2015). Long-term human exposure to various types of DBPs triggers many forms of cancer or other diseases (as presented in Table 1) (Hebert et al.,

2010; Yang and Zhang, 2014; Xiao et al., 2017; Chhetri et al., 2017). The risk to develop cancer (López-Roldán et al., 2016) or diseases caused by THMs ingestion is higher than the risk caused by inhalation during shower or dermal exposure (Dyck et al., 2015). Therefore, water contaminated with DBPs (mostly THMs and HAAs) is highly dangerous for human health and can present high risks if the raw water originates from surface water, and less risks if the source is mixed (e.g., surface water and groundwater or only groundwater). The variety of DBPs known today, caused by the multitude of sources that influence their formation and occurrence, is reflected in the variety and complexity of the negative effects they can have on the environment and humans (Table 1). Some DBPs are considered EPs due to their persistence, low biodegradability and although they can be found in low concentrations, they may have the most devastating effects as compared to other contaminants (Yang and Zhang, 2016).

Because emerging N-DBPs resulted after chlorination or chloramination present cytotoxicity and genotoxicity risks, treatment processes should be applied as described in section 4 (Hu et al., 2018; Chen et al., 2017). With the same toxic characteristics, Br-DBPs resulting during water chlorination and chloramination in the presence of bromide, have a high potential to generate illnesses as compared to Cl-DBPs (Zhang and Yang, 2018). Some classes of DBPs (N-nitrosamines) are classified at international level as substances with a potential risk to develop cancer if the daily ingestion rate is exceeded (Fan and Lin, 2018).

Recent studies focused on formation mechanisms, concentrations and adverse health effects have been conducted those I-aldehydes, cyanides, halonitromethanes, haloketones, haloacetamides, iodinated-DBPs and N-nitrosamines presented in drinking waters are harmful for human health being more cytotoxic, genotoxic and mutagenic than their brominated and chlorinated equivalents (Chen et al., 2018; Andersson et al., 2019, Chaukura et al., 2020). Among N-DBPs, NDMA have received significant attention because low ng/L levels in drinking water are associated with 10^{-6} lifetime excess cancer risks. Epidemiological studies highlight that exposure via inhalation and dermal contact may be

more dangerous than via ingestion of drinking water, because many emerging DBPs are sufficiently volatile such that skin absorption or inhalation during showering can be harmful (Li et al., 2018, Li et al., 2020).

4. Advanced DWT technologies for DBPs prevention and control

Given the number of known DBPs and its continuous growth, to prevent their occurrence and development, operational parameters and drinking water characteristics should be carefully monitored. Implementing technologies that have the ability to remove DBPs and to prevent their re-emergence in the distribution network is highly necessary (López-Roldán et al., 2016). Conventional DWT processes needs to be completed with ADWT processes (Du et al., 2017; Ohar et al., 2014; Chaukura et al., 2020) and/or the use of a strong oxidant as final disinfectant (Zainudin et al., 2018). In order to mitigate DBPs formation, dissemination activities oriented to a reduction of precursors or unnecessary pharmaceuticals use among the population could also be effective (Plewa et al., 2010).

Recent studies at pilot and full-scale showed the high performances of ADWT technologies (Hu et al., 2018; Wang et al., 2015; Jurado-Sanchez et al., 2014) (see Table 4), such as: membrane processes, advanced oxidation processes or adsorption on activated carbon and other materials, which were studied from the points of view of: technological performances (mechanism, pollutants removal efficiency), economic, social and environmental performances (Zainudin et al., 2018; Bui et al., 2016). From the chemical, biological and technological point of views, the prevention of DBPs formation may be possible through preventive actions (disinfectant agents used/ removing DBPs precursors through adequate DWT processes) or treatment actions (removing DBPs after their formation). Each treatment stage, like adsorption (GAC, PAC, CNTs, IER), coagulation/flocculation- C/F, AOPs, membrane filtration or integrated technologies), has its own contribution to the ADWT process efficiency. However, combined technologies ensure better drinking water quality, while preventing the development of certain risks from the recurrence of DBPs.

504 **Table 4.** Overview of DBPs removal by ADWT at pilot and full-scale

Treatment process	DBPs monitored	Operational parameters (PS/FS)	Removal efficiency (%)	References
C/F; S; SF	THMs, CH; DCAcAm; TCAcAm; TCNM and DCAN	**(FS)** pH: 6.5 ± 0.2 Contact time: 24 h		Hu J. et al., 2018
PO ($KMnO_4$/O_3/K_2FeO_4/ ClO_2); C/F; S; SF			17.6%, 23.6%, 19.6%, and 14.5%;	
PO ($KMnO_4$/O_3/K_2FeO_4/ ClO_2); C/F; S; SF; GAC filtration/O_3-GAC advanced treatment			45.3%, 51.1%, 49.3%, and 46.1%;	
UV/TiO_2 $UV/Pt/TiO_2$ Fe(0)/Cu(II) UV-L UV-M	Bromate	**(PS)** Reaction time/pH: 90-150 min/1.5-13.5 90 min/ 8.1; 30 min/6-6.5; 60 min/5.1-9.2; 50 min/ 6.8	50-60%; 95-99%; 100%; 35%–45%; 100%	Xiao et al., 2017
1. PO (Cl_2); C/F; SF (sand/anthracite) 2. PO (Cl_2); C/F; GAC filtration	36 DBPs	**(PS)** Contact time: 7.5/15 min; Cl_2 dose:3-6 mg/L	THMs 20%; Halonitroalkanes-58.50%; Haloaldehydes 33.62%; HAAs 28.13%; Haloalkanes 20.46%; Haloketones 13.46%; Nitrosamines 10.23%; Halonitriles -8.82%; Haloalkenes -9.84%; N-DBPs 4.82%; Chlorite 84.95% (GAC), Chlorite 19.55 % (SF)	Fu et al., 2017
Membrane nanofiltration: ESNA 1-LF2; TS80; NF270	NDMA, HNM, and THM	**(PS)** pH: 6-9; Ionic strength: 0.005-0.05 M; Ca^{2+}: 6-60 mg/L	57-83%; 48-87% and 72-97%	Ersan et al., 2016
RWE, PO, pH adjustment (H_2SO_4); C/F ($Al2(SO_4)_3$); SF; O_3, GAC filtration; Cl_2; pH adjustment (H_2SO_4)	THMs ($CHCl_3$ and BDCM); HAAs (MCAA, MBAA, DCAA, DBAA, BCAA, BDCAA, TCAA, TBAA, H)	**(FS)** O_3 dose: 5 - 0.8 mg/L; T: 7.4°C to 21°C; pH 8.02 - 8.8;	79% for $CHCl_3$; 21%for BDCM; 71% for DCAA and TCAA	Papageorgiou et al., 2016
1) C; S; SF; Cl_2 2) C; S; SF; O_3, BAC, Cl_2	DCAcAm	**(FS)** pH: 8,5; Cl_2 dose: 25.5 mg/L; Disinfection time: 24 h	9% in CDWT plant and 76% in ADWT plant	Lin et al., 2016
1) RWE, PO (ClO_2), C,F,S,SF; UF, RO,REM, Cl_2, Tanks, Cl_2 2) RWE, PO (ClO_2), C,F,S,SF; O_3, GAC filtration, Cl_2, Tanks, Cl_2	THMs	**(FS)**	-	López-Roldán et al., 2016
RWE; F ($Al_2(SO_4)_3$); pH adjustment and activated silica; S; SF (anthracite/sand); NH_2Cl; pH correction and Fl	TTHM and HAA5	**(FS)** Contact time 20 min; Bed layer: anthracite 0.56m and sand 0.3m	75%overall reduction for TTHM and HAA5	Delatolla et al., 2015
RWE; PO (Cl_2); C/F (Al_2Cl_3); S; SF; NH_2Cl	10 THMs, 13 HAAs, 6 HNMs, 6 HANs and 11 aldehydes	**(FS)** Cl_2 dose: 0.6–1.0 mg/L); NH_2Cl dose: 2.1–2.6 mg/L; Contact time 24/48 h; pH 3.0–3.5 (H_2SO_4)	Increased concentration in summer seasons along the distribution network: 50% for HAAs and 350% for THMs. Cl_2 , NH_2Cl dose, C/F, and S steps increase DBPs level in warmer seasons	Serrano et al., 2015
RWE; PO (Cl_2); C/F (Al_2Cl_3); S; SF (sand/anthracite); UV (Cl_2; UV; UV/Cl_2;UV/H_2O_2)	THM, HAA, DCAN, BCAN; AOX	**(FS)** Cl_2 dose: 5–10 mg L^{-1}as free chlorine; UV dose: 1800Mj/m^2;	UV/Cl_2: 27 µg L^{-1} for THM and HAA; < 6 µg L^{-1} for DCAN and BACN; 70 µg Cl $L^{-1}$for AOX.	Wang et al., 2015
RWE; C/F (Al2Cl3); S; SF		Contact time: 30/40	UV/Cl2: 50 µg L^{-1} for	

Treatment process	DBPs monitored	Operational parameters (PS/FS)	Removal efficiency (%)	References
(sand/anthracite); UV (Cl_2; UV; UV/Cl_2;UV/H_2O_2)		seconds; pH: 6.5-8.5	THM and 19-24 for HAA; 20-70 µg Cl L^{-1} for AOX	
RWE, PO (O_3), pH adjustment, C/F, SF, O_3, GAC filtration, Cl, pH adjustment	Carbonyl compounds	**(FS)** T: 7.4 - 17.7°C; pH: 8.02 – 8.80 O_3 dose: 0.29-0.52 mg/L;	~80% (15 - 62% on GAC filtration)	Papageorgiou et al., 2014
RWE, PO ($KMnO_4$), C (Al_xCl_3), S, SF (sand + anthracite), NH_2Cl, Tanks, Cl+Fl	35 Carboxylic acids	**(FS)** T:9-28°C; NH_2Cl dose 0.7 mg/L; Contact time 20 min; pH 6-8	6.3 µg/L	Jurado-Sanchez et al., 2014
RWE, C, O_3, UF (ceramic membrane), GAC filtration, Cl	4 THMs, 6 HAAs	**(FS)** Cl_2 dose 1.5 mg/L; O_3 dose 2–5 mg/L; Contact time 120 min;	73% for THMs and 75% for HAAs	Fan et al., 2014
4 DWTPs: RWE; PO (Cl_2), C/F, S, SF, Cl_2	THM4, HAA5	**(FS)** pH: 7.4-8.1;	64.38, 43.94, 52.41 and 51.72 µg/L for THM4; HAA5;	Gad-Allah et al., 2012

Notes and abbreviations: RWE – raw water extraction; PO – pre-oxidation; pH adjustment; C/F – coagulation/flocculation; SF – sand filtration; O_3 – ozonisation; GAC filtration; Cl – chlorination; S – sedimentation; Fl – fluorination; NH_2Cl – chloramination; UF – ultrafiltration; Cl_2 – Chlorination; BAC – Biological Activated Carbon; REM – Remineralisation; RO - Reverse Osmosis; UV - Ultraviolet Disinfection; PS – Pilot scale; FS – Full scale.

Adsorption is often applied due to its low cost and operational simplicity, providing a high quality of treated water. The majority of DWT processes (Table 4), applied at pilot or full scale, include adsorption on GAC with high removal efficiencies for DBPs. For nitrosamines removal from DW sources, GAC filtration shows an increased efficiency of DBPs precursor removal or DBPs formed after the disinfection process (Leavey-Roback et al., 2016; Zhang and Yang, 2018). A new approach has been studied to control the formation of THMs, HAAs, and total organic halogen (TOX) in chlorinated drinking water by targeting intermediate aromatic halogenated DBPs instead of NOM by using GAC adsorption, the applicability of this method being influenced by the source water matrices and disinfection conditions. With different bromide levels in source waters and different chlorination contact times, the TOX removals with this new approach (chlorine disinfection prior to GAC adsorption) were always doubled or more than doubled as compared to those of the traditional approach (GAC adsorption prior to chlorine disinfection) (Jiang et al., 2018). However, the potential to remove some DBPs through GAC obviously decreases with the saturation of the adsorbent

526 (Zainudin et al., 2018). Another disadvantage consists in the need to manage the
527 wastewater resulting from back-washing the GAC filters (Bhatnagar and Sillanpaa, 2017).
528 In a recent study, Lin et al. (2016) showed that biological activated carbon (BAC) filtration is
529 the most popular technology in DWT process, followed by ozonation. They proved that
530 combined advanced processes (O_3+BAC) significantly improve DCAcAm removal. Few full-
531 scale studies on control and removal of DBPs through BAC processes show that HAAs and
532 THMs formation potential was minimized at 57 % and 45 %, respectively, since bromide
533 concentration was higher after biofiltration. This required a higher capacity to inactivate the
534 microorganisms responsible for the DBPs occurrence (Liu et al., 2017). Different
535 coagulation/flocculation processes ($KMnO_4$, O_3, K_2FeO_4, and ClO_2) applied after pre-
536 treatment resulted in DCAN removal efficiencies higher with 12.9 %, 18.0 %, 16.3 % and
537 10.1 %, respectively, compared to conventional DWT. When O_3-GAC was added to the DWT
538 process, the removal efficiencies increased to 48.6 %, 53.0 %, 51.0 %, and 48.5 %,
539 respectively (Hu et al, 2018).
540 Photocatalytic technologies applied for bromate degradation from post-ozonation showed
541 good reduction efficiency, stable performance and easy combination with UV disinfection
542 techniques (UV/TiO_2; UV/SO_3^{2-}; $UV/Pt/TiO_2$) (Xiao et al., 2017). AOPs with ozone (O_3),
543 hydrogen peroxide (H_2O_2), UV radiation or combinations of these are often used for DBPs
544 removal and recording positive results in DWT processes. Advanced disinfection techniques
545 such as UV or UV/hydrogen peroxide can interact with pharmaceuticals and form
546 hydroxylated compounds and NDMA or can increase some levels of DBPs after chloramine
547 addition (Postigo and Richardson, 2014; Radjenovic et al., 2012).
548 Membrane filtration is often applied for DBPs removal due to the high removal efficiency
549 especially towards THMs precursors (Sutherland et al., 2015). Ultrafiltration (UF), reverse
550 osmosis (RO), advanced oxidation water treatment by post-ozonation and biological
551 activated carbon (BAC) were demonstrated to have a significant contribution in THMs and
552 HAAs removal from drinking water (Lou et al., 2010; Fan et al., 2014). The removal of DBP

553 precursors is influenced by the presence of bacteria, micropollutants and membrane
554 characteristics. For example, chloroform is easily removed using a UF membrane rather than
555 NF or RO membranes (Bodzek et al., 2002). Different membrane technologies (MF, NF, UF,
556 RO) (Fan et al., 2014; Ersan et al., 2016; López-Roldán et al., 2016) proved their efficiency
557 in DBPs removal (see Table 4), however there is a lack of data regarding the application of
558 membrane processes at pilot or full scale and the operational costs (imposed by the rapid
559 fouling of the membranes), high electricity consumption etc. are not available (Zainudin et
560 al., 2018).
561 Considering a critical assessment of the ADWT processes analysed (see Table 4),
562 integrated technologies involving membrane processes present higher removal rates for
563 DBPs or precursors compared to single DWT processes. In the case of THM removal, the
564 efficiency sequence follows the order: O_3/BGAC > GAC; O_3/UF > UF and GAC/SF > SF
565 (Zainudin et al., 2018). However, as a general principle, the benefits of a particular
566 technology applied in a DWT process outline are related to the operational parameters
567 adopted. Once applied a certain technology, a number of challenges arise, especially
568 regarding the quality of water supplied to consumers, which must comply with legislation. At
569 the same time, the performance of a treatment technology may be different from plant to
570 plant. Depending on where any specific technology is implemented within the treatment
571 process, it may influence positively or negatively the quality of the water required for human
572 consumption.
573
574 **5. Conclusions**
575 DWT plants monitoring and management may not fully cover the regulated DBPs occurrence
576 and the further exposure of humans through drinking water consumption. DBPs and their
577 precursors removal from treated water is the key to supply safe drinking water. Unlike the
578 removal of commonly known precursors, which has been greatly developed, up-to-date
579 treatment processes may be not efficient in removing emerging DBPs because of the lack of

580 data on their trace concentrations and the risks associated with these compounds. DBPs
581 removal using a single treatment technology is likely not the best approach for their removal
582 from drinking water. It is necessary to investigate the use of coupled/integrated systems,
583 which can improve the effectiveness of single technologies for the removal of these complex
584 contaminants. The key findings of this study are summarised below.
585 Firstly, operational parameters such as pH, temperature, disinfectant dose, reagents used,
586 and raw water quality should be carefully analysed and optimized to reduce or remove
587 emerging DBPs in order to comply with current standards and regulations. Secondly, the
588 occurrence of DBPs in drinking water due to their persistence, low biodegradability and
589 concentrations, and the pathways related to population exposure may have the most
590 devastating effects against the human body (particularly, the nervous and reproductive
591 systems) for a long time.
592 This study represents a solid foundation for further research, and it highlights the strengths
593 and weaknesses of DWT systems, according to their operational parameters. Due to the
594 multitude of DBPs known and their newly discovered health effects, the analytical methods
595 must be continuously improved. A particularity of this review paper is that only the ADWT
596 technologies for DBPs removal from drinking water sources applied at the pilot or full-scale
597 were considered. It was found that a limited number of studies have been performed in this
598 direction. Various treatment technologies, including membrane processes, advanced
599 oxidation processes and adsorption on activated carbon or other materials have found
600 application at pilot and full-scale, and their selection among available existing mature
601 technologies was mainly based on technical operation conditions and economic
602 considerations. According to the studied literature, the treatment processes that are efficient
603 for DBPs removal from drinking water sources are ADWTs combining different treatment
604 technologies, because every raw water source has individual characteristics and from this
605 point of view, the technological treatment scheme should be specifically adapted to improve
606 the DBPs' removal efficiencies.

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References

1. Alexandrou, L., Meehan, B.J., Jones, O.A.H. 2018. Regulated and emerging disinfection by-products in recycled waters. Sci Total Environ. 637–638, 1607-1616.

2. Ali, M., 2013. Monitoring of some disinfection by-products in drinking water treatment plants of El-Beheira Governorate, Egypt. Appl. Water Sci. 3(4):733–740.

3. Al-Otoum, F., Al-Ghouti, M.A., Ahmed, T.A., Abu-Dieyeh, M., Ali, M., 2016. Disinfection by-products of chlorine dioxide (chlorite, chlorate, and trihalomethanes): Occurrence in drinking water in Qatar. Chemosphere. 164, 649–656.

4. Alver, A., Baştürk, E. and Kılıç, A., 2018. Disinfection By-Products Formation Potential Along the Melendiz River, Turkey; Associated Water Quality Parameters and Non-Linear Prediction Model. Int J Environ Res. 12, 909–919.

5. Alves de Lima, R.O., Bazo, A.P., Salvadori, D.M.F., Rech, C.M., de Palma Oliveira, D., de Aragão Umbuzeiro, G., 2007. Mutagenic and carcinogenic potential of a textile azo dye processing plant effluent that impacts a drinking water source. Mutat Res. 626, 53–60.

6. Andersson A., Ashiq M.J., Shoeb M., Karlsson S., Bastviken D., Kylin H., 2019. Evaluating gas chromatography with a halogen-specific detector for the determination of disinfection by-products in drinking water, Environ. Sci. Pollut. Res. Int. 26, 7305–7314.

7. Barceló, D., 2012. Emerging Organic Contaminants and Human Health, Handb Environ Chem. Springer Berlin Heidelberg, Berlin, Heidelberg. doi:10.1007/978-3-642-28132-7.

636 8. Bereskie, T., Haider, H., Rodriguez, M.J., Sadiq, R., 2017. Framework for continuous
637 performance improvement in small drinking water systems. Sci Total Environ. 574; 1405–
638 1414.

639 9. Bhatnagar, A. and Sillanpaa, M., 2017. Removal of natural organic matter (NOM) and
640 its constituents from water by adsorption - A review. Chemosphere. 166, 497-510.

641 10. Bodzek, M., Waniek, A., Konieczny, K., Desalination 2002. Pressure driven membrane
642 techniques in the treatment of water containing THMs. Desalination 147, 1–3, 101-107.

643 11. Bond, T., Huang, J., Templeton, M.R., Graham, N., 2011. Occurrence and control of
644 nitrogenous disinfection by-products in drinking water – A review. Water Res. 45, 4341–
645 4354.

646 12. Bond, T., Kamal, N.H.M., Bonnisseau, T., Templeton, M.R., 2014. Disinfection by-
647 product formation from the chlorination andchloramination of amines. J Hazard Mater. 278;
648 288–296.

649 13. Bourgin, M., Borowska, E., Helbing, J., Hollender, J., Kaiser, H.P., Kienle, C., McArdell,
650 C.S., Simon, E., von Gunten, U., 2017. Effect of operational and water quality parameters on
651 conventional ozonation and the advanced oxidation process O3/H2O2: Kinetics of
652 micropollutant abatement, transformation product and bromate formation in a surface water.
653 Water Res. 122: 234-245.

654 14. Bruzzoniti, M.C., Rivoira, L., Meucci, L., Fungi, M., Bocina, M., Binetti, R., Castiglioni,
655 M., 2019. Towards the revision of the drinking water directive 98/83/EC. Development of a
656 direct injection ion chromatographic-tandem mass spectrometric method for the monitoring
657 of fifteen common and emerging disinfection by-products along the drinking water supply
658 chain, J Chromatogr A. 1605, 360350.

659 15. Bui, X.T., Vo, T.P.T., Ngo, H.H., Guo, W.S., Nguyen, T.T., 2016. Multicriteria
660 assessment of advanced treatment technologies for micropollutants removal at large-scale
661 applications. Sci Total Environ. 563–564, 1050–1067.

662 16. Canadian DWQ [WWW Document], 2019. Guidel. Can. Drink. Water Qual. Summ.
663 Table Prep. by Fed. Comm. Drink. Water Fed. Comm. Heal. Environmen. URL:
664 https://www.canada.ca/content/dam/hc-sc/migration/hc-sc/ewh-
665 semt/alt_formats/pdf/pubs/water-eau/sum_guide-res_recom/sum_guide-res_recom-eng.pdf.

666 17. Cao, W.C., Zeng, Q., Luo, Y., Chen, H.X., Miao, D.Y., Li, L., et al., 2016. Blood
667 biomarkers of late pregnancy exposure to trihalomethanes in drinking water and fetal growth
668 measures and gestational age in a Chinese cohort. Environ Health Persp. 124, 536–541.

669 18. Chau, H. T. C., Kadokami, K., Duong, H. T., Kong, L., Nguyen, T. T., Nguyen, T. Q.,
670 Ito, Y., 2015. Occurrence of 1153 organic micropollutants in the aquatic environment of
671 Vietnam. Environ Sci Pollut R. doi:10.1007/s11356-015-5060-z.

672 19. Chaukura, N., Marais, M.M., Moyo, W., Mbali, N., Thakalekoala, L.K., Ingwani, T.,
673 Mamba, B.B., Jarvis, P., Nkambule, T.T.I., 2020. Contemporary issues on the occurrence
674 and removal of disinfection byproducts in drinking water - A review. J. Environ. Chem. Eng.
675 8, 103659.

676 20. Chaves, R.S., Guerreiro, C.S., Cardoso, V.V., Benoliel, M.J., Santos, M.M., 2019.
677 Hazard and mode of action of disinfection by-products (DBPs) in water for human
678 consumption: Evidences and research priorities: Review. Comp Biochem Physiol C. 223,
679 53–61.

680 21. Chaves, R. S., Guerreiro, C. S., Cardoso, V. V., Benoliel, M. J., Santos, M. M., 2020.
681 Hazard and mode of action of disinfection by-products (DBPs) in water for human
682 consumption: Evidences and research priorities. Review. Toxicol. Pharmacol. 223, 53-61.

683 22. Chen, H., Lin, T., Chen, W., Tao, H., 2019. Different removal efficiency of disinfection-
684 byproduct precursors between dichloroacetonitrile (DCAN) and dichloroacetamide
685 (DCAcAm) by up-flow biological activated carbon (UBAC) process. Environ Sci Pollut R. 26,
686 25874–25882.

687 23. Chen, T.-L., Tzing, S.-H., Ding W.-H., 2015. Rapid screening of haloacetamides in
688 water using salt-assisted liquid-liquid extraction coupled injection-port silylation gas
689 chromatography-mass spectrometry. J Chromatogr A. 1422: 340-344.

690 24. Chen, W., Liu, Z., Tao, H., Xua, H., Gua, Y., Chen, Z., Yu, J., 2017. Factors affecting
691 the formation of nitrogenous disinfection by-products during chlorination of aspartic acid in
692 drinking water. Sci Total Environ. 575, 519–524.

693 25. Chen, Y., Xu, T., Yang, X., Chu, W., Hu, S., Yin D., 2019, The toxic potentials and
694 focus of disinfection byproducts based on the human embryonic kidney (HEK293) cell
695 model, Sci Total Environ 664, 948–957.

696 26. Chen S., Deng J., Li L., Gao N., 2018. Evaluation of disinfection by-product formation
697 during chlor(am)ination from algal organic matter after UV irradiation, Environ. Sci. Pollut.
698 Res. Int. 25, 5994–6002.

699 27. Chhetri, R.K., Baun, A., Andersen, H.R., 2017. Algal toxicity of the alternative
700 disinfectants performic acid (PFA), peracetic acid (PAA), chlorine dioxide (ClO2) and their

701 by-products hydrogen peroxide (H2O2) and chlorite (ClO2-). Int. J. Hyg. Environ. Health.
702 220(3): 570-574.

703 28. Chowdhury, I.R., Chowdhury, S., Al-Suwaiyan M.S., 2020, Human exposure and risk of
704 trihalomethanes during continuous showering events, Sci Total Environ. 701, 134521.

705 29. Chowdhury, S. Chowdhury, I.R., Zahir, H., 2017, Trihalomethanes in Desalinated
706 Water: Human Exposure and Risk Analysis, Hum. Ecol. Risk Assess. DOI:
707 10.1080/10807039.2017.1362543.

708 30. Chowdhury, S., Rodriguez, M.J., Sadiq, R., 2011. Disinfection byproducts in Canadian
709 provinces: Associated cancer risks and medical expenses. J Hazard Mater. 187, 574–584.

710 31. Chu, W., Gao, N., Yin, D., Krasner, S.W., Templeton, M.R., 2012. Trace determination
711 of 13 haloacetamides in drinking water using liquid chromatography triple quadrupole mass
712 spectrometry with atmospheric pressure chemical ionization. J Chromatogr A. 1235, 178-81.

713 32. Chu, W.H., Gao, N.Y., Deng, Y., Templeton, M.R., Yin, D.Q., 2011. Formation of
714 nitrogenous disinfection by-products from pre-chloramination. Chemosphere. 85(7):1187-91.

715 33. Cojocariu, C., Postigo, C., Richardson, S.D., Barcelo, D., Silcock, P., 2016. Discovery
716 of Emerging Disinfection By-Products in Water Using Gas Chromatography Coupled with
717 Orbitrap-based Mass Spectrometry. Braz. J. Anal. Chem. 6 (22): 98-105

718 34. Corbel, S., Mougin, C., Bouaïcha, N., 2014. Cyanobacterial toxins: Modes of actions,
719 fate in aquatic and soil ecosystems, phytotoxicity and bioaccumulation in agricultural crops.
720 Chemosphere. 96, 1-15.

721 35. Cordero, J.A., He, K., Okuta, E. Echigo, S., Itoh, S., 2020. Effect of biodegradation on
722 haloacetic acid formation potentials of anthropogenic compounds during chlorination.
723 Environ Sci Pollut R. https://doi.org/10.1007/s11356-020-08125-4;

724 36. Dad, A., Jeong, C.H., Wagner, E.D., Plewa, M.J., 2018. Haloacetic Acid Water
725 Disinfection Byproducts Affect Pyruvate Dehydrogenase Activity and Disrupt Cellular
726 Metabolism. Environ Sci Technol. 52(3): 1525-1532.

727 37. de Vera, G.A., Gernjak, W., Weinberg, H., Farre, M. J., Keller, J., Vvon Gunten, U.,
728 2017. Kinetics and mechanisms of nitrate and ammonium formation during ozonation of
729 dissolved organic nitrogen. Water Res. 108:451–461.

730 38. De Vera, G.A., Stalter, D., Gernjak, W., Weinberg, H.S., Keller, J., Farré, M.J., 2015.
731 Towards reducing DBP formation potential of drinking water by favouring direct ozone over
732 hydroxyl radical reactions during ozonation. Water Res. 87:49-58.

733 39. Delatolla, R., Séguin, C., Springthorpe, S., Gorman, E., Campbell, A., Douglas, I.,
734 2015. Disinfection byproduct formation during biofiltration cycle: Implications for drinking
735 water production. Chemosphere. 136:190-7.

736 40. Di Cristo, C., Leopardi, A., Quintiliani, C., de Marinis, G., 2015. Drinking water
737 vulnerability assessment after disinfection through chlorine. Procedia Engineer. 119, 389 –
738 397.

739 41. Diana. M., Felipe-Sotelo, M. and Bond, T., 2019. Disinfection byproducts potentially
740 responsible for the association between chlorinated drinking water and bladder cancer: A
741 review. Water Res. 162, 492-504.

742 42. Ding S., Deng Y., Bond T., Fang C., Cao Z., Chu W. 2019. Disinfection byproduct
743 formation during drinking water treatment and distribution: A review of unintended effects of
744 engineering agents and materials, Water Res. 160, 313-329.

745 43. Ding, S. and Chu, W., 2017. Recent advances in the analysis of nitrogenous
746 disinfection by-products. Trends Environ. Anal. Chem. 14; 19–27.

747 44. Ding, S., Deng, Y., Bond, T., Fang, C., Cao, Z., Chu, W., 2019. Disinfection byproduct
748 formation during drinking water treatment and distribution: A review of unintended effects of
749 engineering agents and materials. Water Res. 160, 313-329.

750 45. Directive 98/83/EC [WWW Document], 1998. Dir. 98/83/EC — Qual. water Intend.
751 Hum. Consum. URL http://eur-lex.europa.eu/legal-
752 content/EN/TXT/?uri=CELEX:31998L0083.

753 46. Dong. F., Liu, J.,Li, C., Lin, Q., Zhang, T., Zhang, K., Sharma, V. K., 2019. Ferrate(VI)
754 pre-treatment and subsequent chlorination of blue-green algae: Quantification of disinfection
755 byproducts. Environ Int. 133, Part B, 105195.

756 47. Du, Y., Lv, X.-T., Wu, Q.-Y., Zhang, D.-Y., Zhou, Y.-T., Peng, L., Hu, H.-Y., 2017.
757 Formation and control of disinfection byproducts and toxicity during reclaimed water
758 chlorination: A review. J Environ Sci. 58, 51-63.

759 48. Duirk, S.E., Collette, T.W., 2006. Degradation of chlorpyrifos in aqueous chlorine
760 solutions: pathways, kinetics, and modelling. Environ Sci Technol. 40, 546–51.

761 49. Dyck R., Cool G., Rodriguez M., Sadiq R., 2015. Treatment, residual chlorine and
762 season as factors affecting variability of trihalomethanes in small drinking water systems.
763 Front Env Sci Eng. 9(1), 171–179.

764 50. Ersan, M.S., Ladner D.A., Karanfil, T., 2016. The control of N-nitrosodimethylamine,
765 Halonitromethane, and Trihalomethane precursors by Nanofiltration. Water Res. 105, 274-
766 281.

767 51. Fan, C.-C. and Lin, T.-F., 2018. N-nitrosamines in drinking water and beer: Detection
768 and risk assessment. Chemosphere. 200:48-56.

769 52. Fan, X., Tao, Y., Wang, L., Zhang, X., Lei, Y., Wang, Z., Noguchi H., 2014.
770 Performance of an integrated process combining ozonation with ceramic membrane ultra-
771 filtration for advanced treatment of drinking water. Desalination. 335, 47–54.

772 53. Feretti, D., Zerbini, I., Ceretti, E., Villarini, M., Zani, C., Moretti, M., Fatigoni, C., Orizio,
773 G., Donato, F., Monarca, S., 2008. Evaluation of chlorite and chlorate genotoxicity using
774 plant bioassays and in vitro DNA damage tests. Water Res. 42(15):4075-82.

775 54. Fu, J., Lee, W.N., Coleman, C., Nowack, K., Carter, J., Huang, C.H., 2017. Removal of
776 disinfection byproduct (DBP) precursors in water by two-stage biofiltration treatment. Water
777 Res. 123: 224-235.

778 55. Gad-Allah, T.A., Badawy, M.I., Abd El-Aty, A.M., Ali, M.E.M., Yoon, Y., 2012.
779 Evaluation of Algal Count and Disinfection By-Products Levels in Drinking Water Treatment
780 Plants in Greater Cairo. J Appl Sci Res. 8(11): 5504-5511.

781 56. Garcia-Villanova, R.J.,Oliveira Dantas Leite, M.V., Hernández Hierro, J.M., de Castro
782 Alfageme, S., García Hernández, C., 2010. Occurrence of bromate, chlorite and chlorate in
783 drinking waters disinfected with hypochlorite reagents. Tracing their origins. Sci Total
784 Environ. 408(12):2616-20.

785 57. Gates, D., Ziglio, G., Ozekin, K., 2009. State of the science of chlorine dioxide in
786 drinking water. Water Research Foundation and Fondazione AMGA.

787 58. GB 5749-2006 [WWW Document], 2007. . Natl. Stand. People's Repub. China.
788 Replace GB 5749-1985. URL: http://www.iwa-network.org/filemanager-
789 uploads/WQ_Compendium/Database/Selected_guidelines/016.pdf.

790 59. Gonsioroski, A., Mourikes, V.E., Flaws, J.A, 2020, Endocrine Disruptors in Water and
791 Their Effects on the Reproductive System, Int. J. Mol. Sci. 21, 1929;
792 doi:10.3390/ijms21061929.

793 60. Goslan, E.H., Seigle, C., Purcell, D., Henderson, R., Parsons, S.A., Jefferson, B., Judd,
794 S.J. 2017. Carbonaceous and nitrogenous disinfection by-product formation from algal
795 organic matter. Chemosphere. 170, 1-9.

796 61. Gougoutsa, C., Christophoridis, C., Zacharis, C.K., Fytianos, K., 2016. Assessment,
797 modelling and optimization of parameters affecting the formation of disinfection by-products
798 in water. Environ Sci Pollut R. 23, 16620–16630.

799 62. Grace, M.A., Clifford, E., Healy, M.G., 2016. The potential for the use of waste products
800 from a variety of sectors in water treatment processes. Review. J Clean Prod. 137, 788-802.

801 63. Guilherme, S., Rodriguez, M.J., 2014. Occurrence of regulated and non-regulated
802 disinfection by-products in small drinking water systems. Chemosphere. 117, 425–432.

803 64. Guilherme, S., Rodriguez, M.J., 2015. Short-term spatial and temporal variability of
804 disinfection by-product occurrence in small drinking water systems. Sci Total Environ. 518–
805 519; 280–289.

806 65. Gupta, V.K., Ali, I., 2013. Front Matter, Environmental Water: Advances in Treatment,
807 Remediation and Recycling. Amsterdam; Heidelberg: Elsevier. doi:10.1016/B978-0-444-
808 59399-3.01001-1.

809 66. Guyton, K.Z., Rusyn, I., Chiu, W.A., Corpet, D.E., van den Berg, M., Ross, M.K.,
810 Christiani, D.C., Beland, F.A., Smith, M.T., 2018. Application of the key characteristics of
811 carcinogens in cancer hazard identification. Carcinogenesis. 39(4): 614–622.

812 67. Han, J., Zhang, X., Liu, J., Zhu, X., Gong, T., 2017. Characterization of halogenated
813 DBPs and identification of new DBPs trihalomethanols in chlorine dioxide treated drinking
814 water with multiple extractions. J Environ Sci. 58, 83-92.

815 68. Hanigan, D., Ferrer, I., Thurman, E.M., Herckes, P., Westerhoff, P., 2017. LC/QTOF-
816 MS fragmentation of N-nitrosodimethylamine precursors in drinking water supplies is
817 predictable and aids their identification. J Hazard Mater. 323(Pt A):18-25.

818 69. Hao, R., Zhang, Y., Du, T., Yang, L., Adeleye, A.S., Li, Y.,2016. Impact of water
819 chemistry on disinfection by-products formation in the complex surface water system,
820 Chemosphere. doi: 10.1016/j.chemosphere.2016.12.034.

821 70. Hebert, A., Forestier, D., Lenes, D., Benanou, D., Jacob, S., Arfi, C., Lambolez, L.,
822 Levi, Y., 2010. Innovative method for prioritizing emerging disinfection by-products (DBPs) in
823 drinking water on the basis of their potential impact on public health. Water Res. 44, 3147–
824 3165.

825 71. Heeb, M.B., Kristiana, I., Trogolo, D., Arey, J.S., von Gunten, U., 2017. Formation and
826 reactivity of inorganic and organic chloramines and bromamines during oxidative water
827 treatment. Water Res. 110:91–101.

828 72. Holmes, B.E., Smeester, L., Fry, R.C., Weinberg, H.S., 2017. Identification of endocrine
829 active disinfection by-products (DBPs) that bind to the androgen receptor. Chemosphere.
830 187, 114-122.

831 73. Hrudey, S.E., Backer, L.C., Humpage, A.R., Krasner, S.W., Michaud, D.S., Moore, L.E.,
832 Singer, P.C., Stanford, B.D., 2015, Evaluating Evidence for Association of Human Bladder
833 Cancer with Drinking-Water Chlorination Disinfection By-Products, J Toxicol Env Heal B:
834 Critical Reviews, DOI: 10.1080/10937404.2015.1067661.

835 74. Hu, J., Chu, W., Sui, M., Xu, B., Gao, N., Ding, S., 2018. Comparison of drinking water
836 treatment processes combinations for the minimization of subsequent disinfection by-
837 products formation during chlorination and chloramination Chem Eng J. 335, 352–361.

838 75. Hu, J.-Y., Aizawa, T., Ookubo, S., 2002. Products of aqueous chlorination of bisphenol
839 A and their estrogenic activity. Environ Sci Technol. 36, 1980–7.

840 76. Hu, S., Gong, T., Ma, J., Tao, Y., Xian, Q., 2018. Simultaneous determination of
841 iodinated haloacetic acids and aromatic iodinated disinfection byproducts in waters with a
842 new SPE-HPLC-MS/MS method. Chemosphere. 198:147-153.

843 77. Huang, N., Wang, T., Wang, W.-L., Wu, Q.-Y., Li, A., Hu, H.-Y., 2017. UV/chlorine as
844 an advanced oxidation process for the degradation of benzalkonium chloride: Synergistic
845 effect, transformation products and toxicity evaluation. Water Res. 114, 246–253.

846 78. Huang, R., Wang, W., Qian, Y., Boyd, J.M., Zhao, Y., Li, X.-F., 2013. Ultra pressure
847 liquid chromatography-negative electrospray ionization mass spectrometry determination of
848 twelve halobenzoquinones at ng/L levels in drinking water. Anal. Chem. 85(9), 4520-9.

849 79. Ibrahim, H.Z., Abu-Shanab, M.A., 2013. Monitoring of some disinfection byproducts in
850 drinking water treatment plants of El-Beheira Governorate, Egypt. Appl. Water Sci. 3, 733–
851 740.

852 80. Japanese Standards [WWW Document], 2016. Minist. Heal. Labour Welf. URL
853 http://www.mhlw.go.jp/english/policy/health/water_supply/dl/4a.pdf.

854 81. Jiang, J., Han, J., & Zhang, X., 2020. Nonhalogenated Aromatic DBPs in Drinking
855 Water Chlorination: A Gap Between NOM and Halogenated Aromatic DBPs. Environ Sci
856 Technol. DOI: 10.1021/acs.est.9b06403;

857 82. Jiang, J., Li, W., Zhang, X., Liu, J., Zhu, X., 2018. A new approach to controlling
858 halogenated DBPs by GAC adsorption of aromatic intermediates from chlorine disinfection:
859 Effects of bromide and contact time. Sep Purif Technol. 203, 260–267;

83. Jiang, J., Zhang, X., Zhu, X., & Li, Y., 2017. Removal of Intermediate Aromatic Halogenated DBPs by Activated Carbon Adsorption: A New Approach to Controlling Halogenated DBPs in Chlorinated Drinking Water. Environ Sci Technol. 51(6), 3435–3444;

84. Jiang, J.-Q., 2013. The Role of Ferrate(VI) in the Remediation of Emerging Micro Pollutants. Procedia Environ Sci. 18, 418–426.

85. Jiang, Y., Goodwill, J.E., Tobiason, J.E., Reckhow, D.A., 2016. Bromide oxidation by ferrate(VI): The formation of active bromine and bromate. Water Res. 96; 188 – 197.

86. Jones, R.R., DellaVallea, C.T., Weyerb, P.J., Robienc, K., Cantora, K.P., Krasnerd, S., Beane Freemana, L.E., Warda, M.H., 2019, Ingested nitrate, disinfection by-products, and risk of colon and rectal cancers in the Iowa Women's Health Study cohort, Environ. Int. 126, 242–25.

87. Jurado-Sánchez, B., Ballesteros, E., Gallego, M., 2014. Occurrence of carboxylic acids in different steps of two drinking-water treatment plants using different disinfectants. Water Res. 51, 186–197.

88. Kaplan, S., 2013. Review: Pharmacological Pollution in Water. Crit Rev Env Sci Tec. 43, 1074–1116.

89. Karanfil, T., Krasner, S.W., Westerhoff, P., Xie, Y., 2008. Recent Advances in Disinfection By-Product Formation, Occurrence, Control, Health Effects, and Regulations. pp. 2–19.

90. Kimura S.Y.,Ortega-Hernandez A.O. 2019. Formation mechanisms of disinfection byproducts: Recent developments, Curr Opin Environ Sci Health. 7: 61-68.

91. Kodamatani, H., Yamasaki, H., Sakaguchi, T., Itoh, S., Iwaya, Y., Saga, M., Saito, K., Kanzaki, R., Tomiyasu, T., 2016. Rapid method for monitoring N-nitrosodimethylamine in drinking water at the ng/L level without pre-concentration using high-performance liquid chromatography-chemiluminescence detection. J Chromatogr A. 1460: 202-6.

92. Kogevinas, M., Bustamante, M., Gracia-Lavedán, E., Ballester, F., Cordier, S., Costet, N., Espinosa, A., Grazuleviciene, R., Danileviciute, A., Ibarluzea, J., Karadanelli, M., Krasner, S., Patelarou, E., Stephanou, E., Tardón, A., Toledano, M.B., Wright, J., Villanueva, C.M., Nieuwenhuijsen, M., 2016. Drinking Water Disinfection By-products, Genetic Polymorphisms, and Birth Outcomes in a European Mother–Child Cohort Study. Epidemiology. 27, 903–911.

891 93. Kolkman, A., Martijn, B.J., Vughs, D., Baken, K.A., van Wezel, A.P., 2015. Tracing
892 nitrogenous disinfection byproducts after medium pressure UV water treatment by stable
893 isotope labeling and high resolution mass spectrometry. Environ Sci Technol. 49, 4458.

894 94. Kubáň, P., Makarõtševa, N., Kiplagat, I.K., Kaljurand, M., 2012. Determination of five
895 priority haloacetic acids by capillary electrophoresis with contactless conductivity detection
896 and solid phase extraction preconcentration. J. Sep. Sci. 35, 666–673.

897 95. Leavey-Roback, L.S., Sugar, C.A., Krasner, S.W., Suffet (Mel) I.H., 2016. NDMA
898 formation during drinking water treatment: A multivariate analysis of factors influencing
899 formation. Water Res. 95, 300-309.

900 96. Lee, C., Lee, Y., Schmidt, C., Yoon, J., Von Gunten, U., 2008. Oxidation of suspected
901 N-nitrosodimethylamine (NDMA) precursors by ferrate (VI): Kinetics and effect on the NDMA
902 formation potential of natural waters. Water Res. 42, 433–441.

903 97. Lee, J., Lee, S., Jiang, X., 2017. Cyanobacterial Toxins in Freshwater and Food:
904 Important Sources of Exposure to Humans. Annu Rev Food Sci Technol. 8, 281-304.

905 98. Legay, C., Rodriguez, M.J., Sérodes, J.B., Levallois, P., 2010, Estimation of
906 chlorination by-products presence in drinking water in epidemiological studies on adverse
907 reproductive outcomes: A review, Sci Total Environ. 408, 456–472.

908 99. Li R. A, McDonald J.A., Sathasivan A., Khan S.J., 2019. Disinfectant residual stability
909 leading to disinfectant decay and byproduct formation in drinking water distribution systems:
910 A systematic review, Water Res. 153, 335-348.

911 100. Li, X.-F., Hrudey, S.E., Bull, R.J., Reckhow, D.A., Humpage, A., Joll, C., Heitz, A.,
912 2011. Analytical Methods for Predicted DBPs of Probable Toxicological Significance [Project
913 #4089].

914 101. Li, X.-F. and Mitch W. A., 2018. Drinking Water Disinfection Byproducts (DBPs) and
915 Human Health Effects: Multidisciplinary Challenges and Opportunities. Environ. Sci. Technol.
916 52, 4, 1681–1689.

917 102. Li, Y., Jiang, J., Li, W., Zhu, X., Zhang, X., Jiang, F., 2020, Volatile DBPs contributed
918 marginally to the developmental toxicity of drinking water DBP mixtures against Platynereis
919 dumerilii. Chemosphere. 252, 126611.

920 103. Li, Y., Shen, W., Fu, S., Yang, H., Yu, G., Wang, Y., 2015. Inhibition of bromate
921 formation during drinking water treatment by adapting ozonation to electro-peroxone
922 process. Chem Eng J. 264; 322–328.

923 104. Lin, T., Zhou, D., Yu, S., Chen W., 2016. The removal process of 2,2-
924 dichloroacetamide (DCAcAm), a new disinfection by-product, in drinking water treatment
925 process and its toxicity on zebrafish. Chemosphere. 159, 403-411.

926 105. Linge, K.L., Kristiana, I., Liew, D., Nottle, C.E., Heitz, A., Joll, C.A., 2017. Formation of
927 N-Nitrosamines in Drinking Water Sources: Case Studies from Western Australia. J Am
928 Water Works Ass. 109, E184–E196.

929 106. Liu, C., Olivares, C.I., Pinto, A.J., Lauderdale, C.V., Brown, J., Selbes, M., Karanfil, T.,
930 2017. The control of disinfection byproducts and their precursors in biologically active
931 filtration processes. Water Res. 124; 630 – 653.

932 107. Liu, J., Lujan, H., Dhungana, B. Hockaday, W.C., Sayes, C.M., Cobb, G.P., Sharma,
933 V.K., 2020, Ferrate(VI) pretreatment before disinfection: An effective approach to controlling
934 unsaturated and aromatic halo-disinfection byproducts in chlorinated and chloraminated
935 drinking waters, Environ. Int. 138, 105641.

936 108. Liu, J., Lujan, H., Dhungana, B., Hockaday, W.C., Sayes, C.M., Cobb, G.P., Sharma,
937 V.K., 2020. Ferrate(VI) pretreatment before disinfection: An effective approach to controlling
938 unsaturated and aromatic halo-disinfection byproducts in chlorinated and chloraminated
939 drinking waters. Environ Int. 138, 105641.

940 109. Liu, W., Zhao, Y., Chow C.W.K., Wang, D., 2011. Formation of disinfection byproducts
941 in typical Chinese drinking water. J Environ Sci. 23(6), 897–903.

942 110. Lodhi, A., Hashmi, I., Nasir, H., Khan, R., 2017. Effect of trihalomethanes (chloroform
943 and bromoform) on human haematological count. J Water Health. 15(3):367-373.

944 111. López-Roldán, R., Rubalcaba, A., Martin-Alonso, J., González, S., Martí, V., Cortina,
945 J.L., 2016. Assessment of the water chemical quality improvement based on human health
946 risk indexes: Application to a drinking water treatment plant incorporating membrane
947 technologies. Sci Total Environ. 540, 334–343.

948 112. Lou, J.-C., Huang, C.-E., Han, J.-Y., Huang, Y.-J., 2010. Generation of disinfection by-
949 products (DBPs) at two advanced water treatment plants. Environ Monit Assess. 162, 365–
950 375.

951 113. Luo, Q., Bei, E., Liu, C., Deng, Y.-L., Miao, Y., Qiu, Y., Lu, W,-Q., Chen, C., Zeng, Q.,
952 2020. Spatial, temporal variability and carcinogenic health risk assessment of nitrosamines
953 in a drinking water system in China. Sci Total Environ. 20, 139695.

954 114. Ma, H., Li, Y., Zhang, H., Shah, S.M., Chen, J., 2014. Salt-assisted dispersive liquid-
955 liquid microextraction coupled with programmed temperature vaporization gas
956 chromatography-mass spectrometry for the determination of haloacetonitriles in drinking
957 water. J Chromatogr A. 1358: 14-9.

958 115. Maeng, M., Shahi, N.K., Shin, G., Son, H., Kwak, D., Dockko, S., 2019. Formation
959 characteristics of carbonaceous and nitrogenous disinfection by-products depending on
960 residual organic compounds by CGS and DAF. Environ Sci Pollut R. 26, 34008–34017.

961 116. Matsumoto, M., Kano, H., Suzuki, M., Katagiri, T., Umeda, Y., Fukushima, S., 2016.
962 Carcinogenicity and chronic toxicity of hydrazine monohydrate in rats and mice by two-year
963 drinking water treatment. Regul Toxicol Pharm. 76:63-73.

964 117. Mehrsheikh, A., Bleeke, M., Brosillon, S., Laplanche, A., Roche, P., 2006. Investigation
965 of the mechanism of chlorination of glyphosate and glycine in water. Water Res. 40, 3003–
966 3014.

967 118. Mercier-Shanks, C., Sérodes, J.-B., Rodriguez, M.J., 2013. Spatio-temporal variability
968 of non-regulated disinfection by-products within a drinking water distribution system. Water
969 Res. 47, 3231–3243.

970 119. Montesinos, I. and Gallego, M., 2012. Solvent-minimized extraction for determining
971 halonitromethanes and trihalomethanes in water. J Chromatogr A.1248: 1-8.

972 120. Müller, A., Weiss, S.C., Beißwenger, J., Leukhardt, H.G., Schulz, W., Seitz, W., Ruck,
973 W.K.L., Weber, W.H., 2012. Identification of ozonation by-products of 4- and 5-methyl1H-
974 benzotriazole during the treatment of surface water to drinking water. Water Res. 46: 679-
975 690.

976 121. Neale, P.A. and Leusch, F.D.L., 2019. Assessing the role of different dissolved organic
977 carbon and bromide concentrations for disinfection by-product formation using chemical
978 analysis and bioanalysis. Environ Sci Pollut R. 26, 17100–17109.

979 122. Ng, T.W., Li, B., Chowa, A., Wong, P.K., 2016. Effects of bromide on inactivation
980 efficacy and disinfection byproduct formation in photocatalytic inactivation. J Photoch
981 Photobio A. 324, 145–151.

982 123. Nieuwenhuijsen, M. J., Martinez, D., Grellier, J., Bennett, J., Best, N., Iszatt, N.,
983 Vrijheid, M., Toledano, M.B., 2009. Chlorination disinfection by-products in drinking water
984 and congenital anomalies: review and meta-analyses. Environ Health Persp. 117:1486–
985 1493.

986 124. Nollet, L.M.L., De Gelder, L., 2014. Handbook of Water Analysis, Third Edition. ISBN
987 9781439889640.

988 125. NWQMS [WWW Document], 2016. Natl. Water Qual. Manag. Strateg. Aust. Drink.
989 Water Guide. 6 2011 Version 3.3 Update. November. 2016. URL
990 https://www.nhmrc.gov.au/_files_nhmrc/file/publications/nhmrc_adwg_6_version_3.3_2.pdf.

991 126. Ohar, Z., Ostfeld, A., 2014. Optimal design and operation of booster chlorination
992 stations layout in water distribution systems. Water Res. 58, 209-20.

993 127. Orak, N.H., Ozsenturk, T., Topuz, E., Aydin, E., Gurel, M., Genceli, E.A., Pehlivanoglu-
994 Mantas, E., 2019. Effect of disinfection processes and anthropogenic pollutants on
995 comparative formation of trihalomethanes and N-nitrosodimethylamine. Int. J. Environ. Sci.
996 Technol. 16, 4083–4090;

997 128. Pan, Y., Li, W., An, H., Cui, H., Wang, Y., 2016. Formation and occurrence of new
998 polar iodinated disinfection byproducts in drinking water. Chemosphere. 144, 2312–2320.

999 129. Pan, Y., Zhang, X., Zhai, J., 2015. Whole pictures of halogenated disinfection
000 byproducts in tap water from China's cities. Front Env Sci Eng. 9, 121–130.

001 130. Papageorgiou, A., Papadakis, N., Voutsa, D., 2016. Fate of natural organic matter at a
002 full-scale Drinking Water Treatment Plant in Greece. Environ Sci Pollut R. 23, 1841–1851.

003 131. Papageorgiou, A., Voutsa, D., Papadakis, N., 2014. Occurrence and fate of ozonation
004 by-products at a full-scale drinking water treatment plant. Sci Total Environ. 481, 392–400.

005 132. Pardakhti, A.R., Bidhendi, G.R.N., Torabian, A., Karbassi, A., Yunesian, M., 2011.
006 Comparative cancer risk assessment of THMs in drinking water from well water sources and
007 surface water sources. Environ Monit Assess. 179, 499–507.

008 133. Pérez-Pavón, J.-L., Herrero-Martín, S., Pinto, C.G., Cordero, B.M., 2008. Determination
009 of trihalomethanes in water samples: A review. Anal Chim Acta. 629(1-2):6-23.

010 134. Petrovic, M., Farré, M., de Alda, M.L., Perez, S., Postigo, C., Köck, M., Radjenovic, J.,
011 Gros, M., Barcelo, D., 2010. Recent trends in the liquid chromatography–mass spectrometry
012 analysis of organic contaminants in environmental samples. J Chromatogr A. 1217, 4004–
013 4017.

014 135. Plewa, M.J., 2010. Toxic Byproducts generated in disinfected Drinking Water
015 Contaminated with Pharmaceuticals. Final Repot for Illinois/Indiana Sea Grant Collage
016 Program Seed Grant

136. Postigo, C., Richardson, S.D., 2014. Transformation of pharmaceuticals during oxidation/disinfection processes in drinking water treatment. J Hazard Mater. 279, 461–475.

137. Pozzi, R., Bocchini, P., Pinelli, F., Galletti, G.C., 2011. Determination of nitrosamines in water by gas chromatography/chemical ionization/selective ion trapping mass spectrometry J Chromatogr A. 1218(14), 1808-14.

138. Prucek, R., Tuček, J., Kolařík, J., Filip, J., Marušák, Z., Sharma, V.K., Zbořil, R., 2013. Ferrate(VI)-Induced Arsenite and Arsenate Removal by In Situ Structural Incorporation into Magnetic Iron(III) Oxide Nanoparticles. Environ Sci Technol. 47(7):3283-92.

139. Qi, J., Lan, H., Liu, R., Miao, S., Liu, H., Qu, J., 2016. Prechlorination of algae-laden water: The effects of transportation time on cell integrity, algal organic matter release, and chlorinated disinfection byproduct formation. Water Res. 102; 221 – 228.

140. Quintiliani C., Di Cristo C., Leopardi A., 2018. Vulnerability assessment to trihalomethane exposure in water distribution systems, Water 10, 912

141. Radjenovic, J., Farré, M.J., Gernjak, W., 2012. Effect of UV and UV/H 2 O 2 in the Presence of Chloramines on NDMA Formation Potential of Tramadol. Environ Sci Technol. 46, 8356–8364.

142. Regli, S., Chen, J., Messner, M., Elovitz, M.S., Letkiewicz, F.J., Pegram, R.A., Pepping, T.J., Richardson, S.D., Wright J.M., 2015, Estimating Potential Increased Bladder Cancer Risk Due to Increased Bromide Concentrations in Sources of Disinfected Drinking Waters, Environ Sci Technol, 49, 13094−13102.

143. Richardson, S.D., 2005. New disinfection by-product issues: emerging DBPs and alternative routes of exposure. Global NEST 7, 43–60.

144. Richardson, S.D., Postigo, C., 2011. Drinking Water Disinfection By-products. Emerging Organic Contaminants and Human Health. pp. 93–137. doi:10.1007/698_2011_125.

145. Richardson, S.D., Postigo, C., 2016. Discovery of New Emerging DBPs by High-Resolution Mass Spectrometry. Compr. Anal. Chem. 335–356. Doi: 10.1016/bs.coac.2016.01.008

146. Ripollés, C., Pitarch, E., Sancho, J.V., López, F.J., Hernández, F., 2011. Determination of eight nitrosamines in water at the ng $L(^{-1})$ levels by liquid chromatography coupled to atmospheric pressure chemical ionization tandem mass spectrometry. Anal Chim Acta. 702: 62-71.

147. Rivera-Núńez Z., Wright J.M., Meyer A., 2018, Exposure to disinfectant by-products and the risk of stillbirth in Massachusetts, Occup Environ Med. **0**:1–10. doi:10.1136/oemed-2017-104861.

148. Rong, C., Shao, Y., Wang, Y. Zhang, Y., Yu, K., 2018. Formation of disinfection byproducts from sulfamethoxazole during sodium hypochlorite disinfection of marine culture water. Environ Sci Pollut R. 25, 33196–33206.

149. Rubirola, A., Boleda, M.R., Galceran, M.T., Moyano, E., 2019. Formation of new disinfection by-products of priority substances (Directive 2013/39/UE and Watch List) in drinking water treatment. Environ Sci Pollut R. 26, 28270–28283.

150. Salas, L.A., Bustamante,M., Gonzalez, J.R., Gracia-Lavedan, E.,Moreno, V., Kogevinas,M., 2015. DNA methylation levels and long-term trihalomethane exposure in drinking water: an epigenome-wide association study. Epigenetics. 10, 650–661.

151. Selbes, M., Beita-Sandi, W., Kim, D., Karanfil, T., 2018. The role of chloramine species in NDMA formation. Water Res. 140, 100-109;

152. Serrano, M., Montesinos, I., Cardador, M.J., Silva, M., Gallego, M., 2015. Seasonal evaluation of the presence of 46 disinfection by-products throughout a drinking water treatment plant. Sci Total Environ. 517: 246-58.

153. Serrano, M., Silva, M., Gallego, M., 2014. Fast and "green" method for the analytical monitoring of haloketones in treated water. J Chromatogr A. 1358: 232-9.

154. Serrano, M., Silva, M., Gallego, M., 2015. Determination of 14 haloketones in treated water using solid-phase microextraction and gas chromatography-mass spectrometry. J Chromatogr A. 1407: 208-15.

155. Shah, A.D., Mitch, W.A., 2012. Halonitroalkanes, halonitriles, haloamides, and N-nitrosamines: a critical review of nitrogenous disinfection byproduct formation pathways. Environ Sci Technol. 46(1):119-31.

156. Shahi, N. K., Maeng, M. and Dockko, S., 2019. Models for predicting carbonaceous disinfection by-products formation in drinking water treatment plants: a case study of South Korea. Environ Sci Pollut R. https://doi.org/10.1007/s11356-019-05490-7.

157. Sharma, V.K., 2010. Oxidation of nitrogen-containing pollutants by novel ferrate (VI) technology: A review. J Environ Sci Heal A. 45, 645–667.

158. Shen, L., Liao, X., Qi, H., Zhao, L., Li, F., Yuan, B., 2019. NDMA formation from 4,4′-hexamethylenebis (HDMS) during ozonation: influencing factors and mechanisms. Environ Sci Pollut R. 26, 1584–1594;

159. Sillanpää, M., Matilainen, A., 2014. NOM Removal by Advanced Oxidation Processes, Natural Organic Matter in Water: Characterization and Treatment Methods. Elsevier Inc. doi:10.1016/B978-0-12-801503-2.00006-9.

160. Smith, R.B., Edwards, S.C., Best, N., Wright, J., Nieuwenhuijsen, M.J., Toledano, M.B., 2016, Birth Weight, Ethnicity, and Exposure to Trihalomethanes and Haloacetic Acids in Drinking Water during Pregnancy in the Born in Bradford Cohort, Environ Health Perspect 124:681–689; http://dx.doi.org/10.1289/ehp.1409480.

161. Snyder, S.A., Stanford, B.D., Pisarenko, A.N., Gordon, G., Asami, M., 2009. Hypochlorite - An assessment of factors that influence the formation of perchlorate and other contaminants. J Am Water Works Assoc. 1–141.

162. Sorlini, S., Gialdini, F., Biasibetti, M., Collivignarelli, C., 2014. Influence of drinking water treatments on chlorine dioxide consumption and chlorite/chlorate formation, Water Res. 54, 44-52.

163. Susinskis, I., Mekss, P., Hmelnickis, J., 2018. Method development for the determination of 1,1-dimethylhydrazine by the high-performance liquid chromatography-mass spectrometry technique. Eur J Mass Spectrom (Chichester, England) Jan doi:01:1469066718761437.

164. Sutherland, S., Parsons, S.A., Daneshkhah, A., Jarvis, P., Judd, S.J., 2015. THM precursor rejection by UF membranes treating Scottish surface waters. Sep. Purif. Technol. 149, 381-388.

165. Teodosiu, C., Gilca, A.F., Barjoveanu, G., Fiore, S. 2018. Emerging pollutants removal through advanced drinking water treatment: A review on processes and environmental performances assessment, J. Clean. Prod. 197, 1210-1221.

166. Ternes, T., von Gunten, U., 2010. Editorial to special issue in Water Res. Emerging contaminants in water. Water Res. 44, 351.

167. TOXNET [WWW Document], 2018. URL: https://toxnet.nlm.nih.gov/cgi-bin/sis/search2/f?./temp/~UGPJbH:2 (accessed 03.04.2018).

168. Tugulea, A.M., Aranda-Rodriguez, R., Berube, D., Giddinngs, M., Lemieux, F., Hnatiw, J., Dabeka, L., Breton, F., 2018. The influence of precursors and treatment process on the formation of Iodo-THMs in Canadian drinking water. Water Res. 130, 215-223.

169. US EPA [WWW Document], 2009. Table Regul. Drink. Water Contam. URL https://www.epa.gov/sites/production/files/2016-06/documents/npwdr_complete_table.pdf.

170. US-EPA Environmental protection agency, National Primary Drinking Water Regulations: Stage 2 Disinfectants and Disinfection Byproducts, Rule Federal Register. 71 (2006) (Number 2) 387-493.

171. Villanueva, C.M., Cordier, S., Font-Ribera, L., Salas, L.A., Levallois, P., 2015. Overview of Disinfection By-products and Associated Health Effects. Current Environmental Health Reports 2, 107–115.

172. Wang, D., Bolton, J.R., Andrews, S.A., Hofmann, R., 2015. Formation of disinfection by-products in the ultraviolet/chlorine advanced oxidation process. Sci Total Environ. 518–519, 49–57.

173. Wang, W., Moe, B., Li, J., Qian, Y., Zheng, Q., Li, X.-F., 2016. Analytical characterization, occurrence, transformation, and removal of the emerging disinfection byproducts halobenzoquinones in water. Trends in Anal Chem. 85, 97–110.

174. Wang, X., Mao, Y., Tang, S., Yang, H., Xie, Y.F., 2015. Disinfection byproducts in drinking water and regulatory compliance: A critical review. Front Env Sci Eng. 9, 3–15.

175. Wang, Y., Zhu, G., Engel, B., 2019, Health risk assessment of trihalomethanes in water treatment plants in Jiangsu Province, China, Ecotoxicol. Environ. Saf. 170, 346–354.

176. Watson, K., Farré, M.J., Birt, J., McGree, J., Knight, N., 2015. Predictive models for water sources with high susceptibility for bromine-containing disinfection by-product formation: implications for water treatment. Environ Sci Pollut R. 22, 1963–1978.

177. Wei, J., Ye, B., Wang, W., Yang, L., Tao, J., Hang, Z., 2010. Spatial and temporal evaluations of disinfection by-products in drinking water distribution systems in Beijing, China. Sci Total Environ. 408, 4600–4606.

178. WHO [WWW Document], 2006. World Health Organ. Guidel. Drink. Qual. [electronic Resource. Inc. first addendum. Vol. 1, Recomm. – 3rd ed. URL http://www.who.int/water_sanitation_health/dwq/gdwq0506.pdf.

179. WHO [WWW Document], 2008. World Health Organ. Guidel. Drink. Qual. [electronic Resource. Inc. 1st 2nd addenda, Vol.1, Recomm.– 3rd ed. URL http://www.who.int/water_sanitation_health/dwq/fulltext.pdf

180. WHO [WWW Document], 2017. Guidelines for drinking-water quality: fourth edition incorporating the first addendum. ISBN 978-92-4-154995-0 URL

http://www.who.int/water_sanitation_health/publications/drinking-water-quality-guidelines-4-including-1st-addendum/en/.

181. Winid, B., 2015. Bromine and water quality – Selected aspects and future perspectives. Appl Geochem. 63, 413–435.

182. Wu, Q,Y., Yan, Y,-J., Lu, Y., Du, Y., Liang, Z.-F., Hu, H.-Y., 2020. Identification of important precursors and theoretical toxicity evaluation of byproducts driving cytotoxicity and genotoxicity in chlorination. Front Env Sci Eng. 14, Article number: 25, https://doi.org/10.1007/s11783-019-1204-6;

183. Wu, S., Anumol, T., Gandhi, J., Snyder, S.A., 2017. Analysis of haloacetic acids, bromate, and dalapon in natural waters by ion chromatography-tandem mass spectrometry. J Chromatogr A. 1487: 100-107.

184. Xia, Y., Lin, Y.-L., Xu, B., Hu, C.-Y., Gao, Z.-C., Chu, W.-H., Gao, N.-Y., 2017. Iodinated trihalomethane formation during chloramination of iodate containing waters in the presence of zero-valent iron. Water Res. 124; 219-226.

185. Xiao, Q., Yu, S., Li, L., Wang, T., Liao, X., Ye, Y., 2017. An overview of advanced reduction processes for bromate removal from drinking water: Reducing agents, activation methods, applications and mechanisms. J Hazard Mater. 324(Pt B):230-240.

186. Yang, L., Chene, X., Shef, Q., Cao, G., Liu, Y, Chang, V.W.-C., Tangh, C.Y., 2018, Regulation, formation, exposure, and treatment of disinfection by-products (DBPs) in swimming pool waters: A critical review, Environ. Int. 121, 1039–1057.

187. Yang, M. and Zhang, X., 2016. Current trends in the analysis and identification of emerging disinfection byproducts. Trends Environ. Anal. Chem. 10, 24–34.

188. Yang, M., Zhang, X., Liang, Q., Yang, B., 2019. Application of (LC/)MS/MS precursor ion scan for evaluating the occurrence, formation and control of polar halogenated DBPs in disinfected waters: A review. Water Res. 158, 322 - 337;

189. Yang, P., Zhou, B., Cao, W.-C., Wang, Y.-X., Huang, Z., Li, J., Lu, W.-Q., Zeng, Q., 2017. Prenatal exposure to drinking water disinfection by-products and DNA methylation in cord blood. Sci Total Environ. 586, 313–318.

190. Yang, X., Guo, W., Zhang, X., Chen, F., Ye, T., Liu, W., 2013. Formation of disinfection by-products after pre-oxidation with chlorine dioxide or ferrate. Water Res. 47, 5856–5864.

191. Ye, B., Li, J. and Zhang, X., 2019. Advantages of a ClO2/NaClO combination process for controlling the disinfection by-products (DBPs) for high algae-laden water. Environ Geochem Hlth. 41, 1545–1557;

192. Young, T.R., Li, W., Guo, A., Korshin, G.V., Dodd, M.C., 2018. Characterization of disinfection byproduct formation and associated changes to dissolved organic matter during solar photolysis of free available chlorine, Water Res.146, 318-327.

193. Zainudin, F.M., Hasan, H.A., Abdullah, S.R.S., 2018. An overview of the technology used to remove trihalomethane (THM), trihalomethane precursors, and trihalomethane formation potential (THMFP) from water and wastewater. J Ind Eng Chem. 57: 1-14.

194. Zaleschi, L., Teodosiu, C., Cretescu, I., Rodrigo, M.A., 2012. A Comparative Study of Electrocoagulation and Chemical Coagulation Processes Applied for Wastewater Treatment, Environ Eng Manag J. vol. 11, no. 8, p. 1517-1525.

195. Zha, X., Liu, Y., Liu, X., Zhang, Q., Dai, R., Ying, L., Wu, J., Wang, J., Ma, L., 2014. Effects of bromide and iodide ions on the formation of disinfection by-products during ozonation and subsequent chlorination of water containing biological source matters. Environ Sci Pollut R Int. 21, 2714–2723.

196. Zhai, H., He, X., Zhang, Y., Du, T., Adeleye, A.S., Li, Y., 2017. Disinfection byproduct formation in drinking water sources: A case study of Yuqiao reservoir, Chemosphere. doi: 10.1016/j.chemosphere.2017.04.028.

197. Zhai, H., Zhang, X., Zhu, X., Liu, J., Ji, M., 2014. Formation of Brominated Disinfection Byproducts during Chloramination of Drinking Water: New Polar Species and Overall Kinetics, Envir Sci Tech Lib. 48(5), 2579 – 2588;

198. Zhang, H. and Yang, M., 2018. Characterization of brominated disinfection byproducts formed during chloramination of fulvic acid in the presence of bromide. Sci Total Environ. 627,118–124.

199. Zhang, X. Bull, R.J., Fisher, J., Cotruvo, J.A., Cummings, B.S., 2011. The synergistic effect of sodium chlorite and bromochloroacetic acid on $BrO3^{(-)}$-induced renal cell death. Toxicology. 289(2-3):151-9.

200. Zhao, Y., Anichina, J., Lu, X., Bull, R.J., Krasner, S.W., Hrudey, S.E., Li X.-F., 2012. Occurrence and formation of chloro- and bromobenzoquinones during drinking water disinfection. Water Res. 46, 4351-4360.

201. Zhou, S., Xia, Y., Li, T., Yao, T., Shi, Z., Zhu, S., Gao, N., 2016. Degradation of carbamazepine by UV/chlorine advanced oxidation process and formation of disinfection by-products. Environ Sci Pollut R Int. 23(16), 16448-55.

202. Zulkiflia, S.H., Rahima, H.A., Lau, W.-A., 2018. Detection of contaminants in water supply: A review on state-of-the-art monitoring technologies and their applications. Sensor Actuat B-Chem. 255: 2657–2689.