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Review

Parabens as environmental contaminants of aquatic systems affecting water quality and microbial dynamics

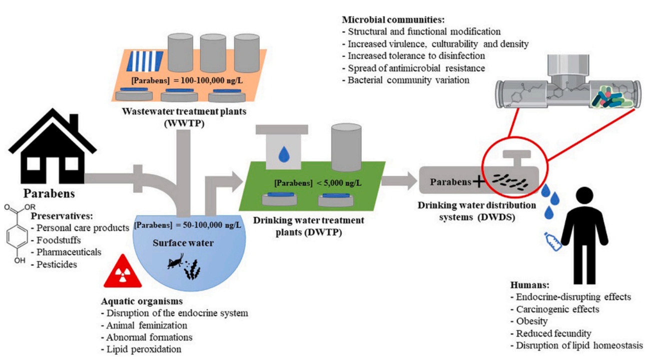
Ana Rita Pereira, Manuel Simões *, Inês B. Gomes *

LEPABE - Laboratory for Process Engineering, Environment, Biotechnology and Energy, Faculty of Engineering, University of Porto, Rua Dr. Roberto Frias, 4200-465 Porto, Portugal
ALiCE - Associate Laboratory in Chemical Engineering, Faculty of Engineering, University of Porto, Rua Dr. Roberto Frias, 4200-465 Porto, Portugal

HIGHLIGHTS

- The extensive use of parabens results in aquatic environmental contamination.
- Parabens are found in drinking water up to 6 μg/L, threatening consumers' health.
- Parabens affect the structure, metabolism and antimicrobial tolerance of biofilms.
- Bacterial exposure to parabens can contribute to the spread of antibiotic resistance.

GRAPHICAL ABSTRACT



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ABSTRACT

Among different pollutants of emerging concern, parabens have gained rising interest due to their widespread detection in water sources worldwide. This occurs because parabens are used in personal care products, pharmaceuticals, and food, in which residues are generated and released into aquatic environments. The regulation of the use of parabens varies across different geographic regions, resulting in diverse concentrations observed globally. Concentrations of parabens exceeding 100 μg/L have been found in wastewater treatment plants and surface waters while drinking water (DW) sources typically exhibit concentrations below 6 μg/L. Despite their low levels, the presence of parabens in DW is a potential exposure route for humans, raising concerns for both human health and environmental microbiota. Although a few studies have reported alterations in the functions and characteristics of microbial communities following exposure to emerging contaminants, the impact of the exposure to parabens by microbial communities, particularly biofilm colonizers, remains largely understudied. This review gathers the most recent information on the occurrence of parabens in water sources, as well as their effects on human health and aquatic organisms. The interactions of parabens with microbial communities are reviewed for the first time, filling the knowledge gaps on the effects of paraben exposure on microbial ecosystems and their impact on disinfection tolerance and antimicrobial resistance, with potential implications for public health.

* Corresponding authors.
E-mail addresses: mvs@fe.up.pt (M. Simões), ibgomes@fe.up.pt (I.B. Gomes).

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Nomenclature

2-Cl-PP	di-chlorinated propylparaben
3,4-DHB	3,4-dihydroxybenzoic acid
3,5-2Cl-EP	3,5-dichloro-4-hydroxybenzoate
4-HB	4-hydroxybenzoic acid
AhR	aryl hydrocarbon receptor
ARBs	antibiotic-resistant bacteria
ARGs	antibiotic-resistant genes
BA	benzoic acid
bacA	bacitracin
BP	butylparaben
Br_2BP	di-brominated butylparaben
Br_2BzP	di-brominated benzylparaben
BzP	benzylparaben
DBPs	disinfection by-products
DW	drinking water
DWDS	drinking water distribution systems
DWTP	drinking water treatment plants
EC_{50}	effective concentration
ECs	emerging contaminants
EFSA	European Food Safety Authority
EP	ethylparaben
EPA	Environmental Protection Agency
EPS	extracellular polymeric substances
ERR γ	estrogen-related receptor γ
EU	European Union
FDA	food and drug administration
GRAS	generally recognized as safe
HepP	heptylparaben
iBP	isobutilparabeno
iPP	isopropylparaben
LC_{50}	lethal concentration
LOD	limit of detection
LOEC	lowest-observed-effect concentration
MBC	minimum bactericidal concentration
MEC	measured environmental concentration
MIC	minimum inhibitory concentration
MP	methylparaben
NOEC	no-observed effect concentration
NOEL	no observable effect level
OH-EP	ethyl protocatechuate
OH-MP	methyl protocatechuate
OmpF	outer membrane protein
PAW	plasma-activated water
PCPs	personal care products
PEC	predicted environmental concentration
p-HBA	p-hydroxybenzoic acid
PhP	phenylparaben
PNEC	predicted no-effect concentration
PP	propylparaben
PtP	pentylparaben
RQ	risk quotient
ROS	reactive oxygen species
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SCCS	Scientific Committee on Consumer Safety
UK	United Kingdom
US	United States
WHO	World Health Organization
WWTP	wastewater treatment plants

1. Introduction

Safe drinking water (DW) is crucial to ensure public health, as highlighted by the United Nations sustainable development goals of Agenda 2030, particularly Goals 3 (Ensure healthy lives and promote well-being for all at all ages) and 6 (Ensure access to water and sanitation for all) (United Nations, 2022). Safe DW is not sterile and contains diverse microorganisms competing for limited available nutrients that in stable conditions do not affect water quality (Prest et al., 2016). In drinking water distribution systems (DWDS), more than 95% of the microorganisms live embedded in extracellular polymeric substances (EPS) of biofilms adhered to the walls of the network (Flemming et al., 2002). The biofilm cell density in DWDS is expected to be in the range of 10^4 to 10^8 cells/cm^2 (Prest et al., 2016). However, deregulations on microbial stability and uncontrolled growth of bacteria can occur during water distribution, disturbing water safety and posing a significant public health concern (Chan et al., 2019).

Aside from microbiological problems, DW is also affected by the presence of emerging contaminants (ECs), whose consequences for DW microbial quality and safety have been disregarded so far. Parabens are an example of these contaminants and are widely used as preservatives and antimicrobial agents in personal care products (PCPs), pharmaceuticals, and food (Soni et al., 2005). Due to the widespread population growth and urbanization, parabens are released into the environment, being their presence in aquatic sources frequently reported (Gomes et al., 2020). Parabens are commonly found in wastewater and surface water sources at elevated concentrations (up to 100 μg/L) and high-frequency detections (up to 90%), reflecting the regulatory status for the use of parabens in each country/region worldwide and the consumption rates of these products (Wei et al., 2021). Moreover, parabens escape from wastewater treatment plants (WWTP) and DW treatment plants (DWTP), so they are still found in DW at trace concentrations ranging from 3 ng/L (Pai et al., 2020) to 6 μg/L (Radwan et al., 2020). Therefore, DW biofilms are microbial communities prone to continuously exposed to parabens contamination. However, studies evaluating the presence of parabens in DW are scarce, likely due to the difficulty to quantify their presence at trace concentrations (ng/L), which requires the use of highly sensitive analytical techniques such as ultra high-performance liquid chromatography, among others (Gomes et al., 2020). Furthermore, the mixture and complexity of chemical compounds presented in DW add another layer of difficulty in the extraction and separation processes (Lincho et al., 2021). Moreover, some of these compounds remain to be identified (Escher et al., 2020).

Due to the need for water disinfection, the simultaneous presence of parabens and chlorine in DWDS may lead to the formation of halogenated compounds that become even more worrying in terms of public health than the pristine parabens, highlighting the need to deeply study these halogenated parabens (Penrose and Cobb, 2022). The presence of parabens in food and PCPs can directly affect human health through absorption, resulting in negative human health concerns such as endocrine-disrupting effects and carcinogenic potential (Błedzka et al., 2014). Like human health effects, continuous exposure to residual concentrations of parabens induces developmental disorders in aquatic organisms (Kang et al., 2019), being potentially toxic to them (Lincho et al., 2021). As parabens are highly dispersed in aquatic ecosystems, environmental microorganisms (including biofilms in DW) are inevitably exposed to these contaminants (Błedzka et al., 2014). Considering that parabens are used as preservatives with known antimicrobial activity, it is important to understand the consequences from the continuous exposure of microorganisms to parabens at sub-inhibitory concentrations. The real mechanism of the antimicrobial action of parabens and consequently, the mode of interaction between parabens and microorganisms remains to be understood (Ito et al., 2015). Nonetheless, it is thought to be related to modifications in bacterial membranes

(Flasiński et al., 2018). There are some studies reporting the impact of ECs on microbial communities in water sources with particular emphasis on the role of pharmaceutical contaminants, but non-pharmaceutical ECs (such as parabens) have received reduced attention (Gomes et al., 2020). Some of these studies reported modifications in biofilm formation (Pinto et al., 2023; Zhang et al., 2021), structure, and composition (Arruda et al., 2022a; Wang et al., 2019a, 2019b). Others highlight changes in the production of virulence factors (Gomes et al., 2019b), promoting antimicrobial resistance spread (Gomes et al., 2019b) and increased tolerance to disinfection (Gomes et al., 2019a, 2019b). However, data on the impact of any type of ECs on DW bacterial communities is still scarce, and there is only one study reporting the impact of parabens in DW biofilms (Pereira et al., 2023). Since environmental microorganisms may affect human health, the impact of parabens on these microbial communities must be addressed. This review provides a critical insight on the presence and identification of parabens in aquatic systems, particularly in DW, assessing the global trends in parabens usage and monitorization in aquatic systems. The latest research findings on the main effects of parabens on human health are described as well as their ecotoxicological effects. This work further compiles for the first time the research evidences on the interactions between parabens (at environmental concentrations) and microorganisms, highlighting their effects on antimicrobial tolerance and the potential implications for public health. Therefore, this review provides pioneer information for water researchers, companies and regulatory entities to critically assess the presence of ECs, particularly parabens, in water sources anticipating potential microbiological-related public health concerns.

2. Parabens as emerging contaminants

Parabens are esters of p-hydroxybenzoic acid (p-HBA) that differ from each other by the type of substituent, which may be an alkyl chain or an aromatic ring (Nowak et al., 2018). The most commonly used parabens are methylparaben (MP), propylparaben (PP), butylparaben (BP) and ethylparaben (EP) (Bolujoko et al., 2021). However, several other parabens are known, including isoPP (iPP), isoBP (iBP), benzylparaben (BzP), phenylparaben (PhP) and pentylparaben (PtP). Parabens are added to a wide variety of consumer products, including commercial dentifrices, sanitary wipes, tickets, newspapers, food packages, and paper currency (Lincho et al., 2021). In the United States (US), MP, EP, and PP were found in bactericidal creams and solutions at 2840, 734, and 278 ng/g, respectively (Gao and Kannan, 2020). Moreover, MP, EP, PP, iPP, BP, and BzP were measured in supermarkets in Vietnam at 3280 and 69.4 μg/g in labeled-PCPs and non-labeled-PCPs, respectively (Tran et al., 2021). The popular use of paraben preservatives in cosmetics and PCPs arises from their favorable properties: small colorless crystals, odorless and tasteless, chemically stable, inertness, reduced toxicity, broad-spectrum action against microorganisms, biodegradability, low cost (Wei et al., 2021) and worldwide regulatory acceptance (Soni et al., 2005). Parabens constitute more than 22,000 types of cosmetics, and it is expected to grow by 8% in the cosmetic industry for the next 6 years (Global Market Insights, 2022), which is the main driver of parabens pollution of aquatic systems (Bilal et al., 2020). This may lead to worrying levels of parabens in different ecosystems and may cause human and animal health complications.

2.1. Regulatory status of parabens

Parabens are used in the cosmetic industry at mg/g and in the food and pharmaceutical industries at ng/g (Wei et al., 2021). Their presence is also widely reported in the environment, specifically in water sources, including in DW, which highlights the importance of regulating their in-use concentration to control the release into the environment (Bolujoko et al., 2021). Although parabens have been produced in high volumes in the European Union (EU), the US, and Asia, the regulation for their use differs across regions and purposes (Wei et al., 2021). Curiously in China, the production rates of MP and EP were as high as 500 tons/month and PP was reported to be >10,000 tons/month (Ministry of Health of the People's Republic of China, 2011). According to the legal standards of the US Food and Drug Administration (FDA) (US Food and Drug Administration, 2022) and EU standards (European Commission, 2011), parabens are classified as generally recognized as safe (GRAS) additives. Risk assessments of parabens in the EU are regulated by the European Food Safety Authority (EFSA) (European Food Safety Authority, 2004) and the Scientific Committee on Consumer Safety (SCCS) (Scientific Committee on Consumer Safety, 2011).

Overall, MP and EP are the most commonly used parabens in the food industry worldwide. In the EU, regulation N° 1130/2011 authorizes the use of MP and EP up to 2 mg/kg in food; 1 mg/L for use in drinks, and 2000 mg/kg in enzyme preparations (Table 1) while PP and BP are not allowed in food or food-contact plastics (European Commission, 2011). In addition, these parabens were prohibited in children's products in Denmark (Scientific Committee on Consumer Safety, 2011). The use of PP as a food additive was banned in the EU in 2006 due to the observed negative effects on male reproductive organs in juvenile rats (Klančič et al., 2022). Moreover, in EU food products, the presence of parabens should be communicated through a label with an E symbol on the wrapper (European Commission, 2011). The EFSA defined the acceptable daily intake for MP, EP and PP as 0–10 mg/kg body weight (European Food Safety Authority, 2004).

However, in the US, the FDA authorized the use of parabens (also including PP) as food additives at a level not to exceed 0.1% of each by weight of the finished food (Soni et al., 2002). This is translated in 1 g/L for drinks and 1 g/Kg in foods, which are much higher values than those standardized for EU (Table 1). Meanwhile, in China, the maximum concentration allowed of MP, EP and PP in food is 0.5 g/kg (Ministry of Health of the People's Republic of China, 2011). MP is the most commonly used in foodstuffs, and Liao et al. (2013) revealed that the highest levels of MP found in Chinese food ingredients were in vegetables (109 ng/g), condiments (75.4 ng/g), and cereals (25.2 ng/g).

Regarding the use of parabens in the cosmetic industry, some modifications in the EU regulations have been made. Regulation N° 358/2014 (European Commission, 2014a) and Regulation N° 1004/2014 (European Commission, 2014b) updated the standards of parabens concentration in the cosmetic industry on EU markets and banned iPP, iBP, PhP, BzP and PtP from it. However, MP and EP can still be used up

Table 1
Maximum concentrations allowed for parabens in different industries and regions.

	Food industry	Cosmetic industry	Pharmaceuticals industry	References
European Union	$<2 \times 10^{-3}$ g/kg food 1 mg/L drinks 2 g/kg enzyme	- MP and PP < 0.4% each and 0.8% in combination - PP and BP < 0.14% in combination	1%	(European Commission, 2011, 2014a, 2014b; European Food Safety Authority, 2004; Scientific Committee on Consumer Safety, 2011)
United States	1 g/kg food 1 g/L drinks	Without restrictions	Without restrictions	(US Food and Drug Administration, 2022)
China	0.5 g/kg food	Without restrictions	Without restrictions	(Ministry of Health of the People's Republic of China, 2011)

to 0.4% and 0.8%, respectively, either individually or in a mixture. PP and BP have individual concentration limits of 0.14% and a combined limit of 0.8% when used with MP and EP. PP and BP remain prohibited in children's products (European Commission, 2014b). Interestingly, the US and China allow the use of parabens in cosmetics without restrictions (US Food and Drug Administration, 2022), while in Japan parabens are allowed to be used in cosmetic products up to 1% (Lincho et al., 2021).

In terms of pharmaceutical products, the maximum concentration of parabens allowed in the EU is around 1%, and information about the presence of parabens must be provided (Soni et al., 2001). MP and PP can be used in oral formulation in the range between 0.015 and 0.2% and 0.01–0.02%, respectively (Lincho et al., 2021). The use of PP is restricted to a No Observable Effect Level (NOEL) of 100 mg/kg/day, due to its associated estrogenic effects whereas the use of MP in pharmaceutical formulations is not restricted (European Medicines Agency, 2015). There is a lack of information about the use of parabens in pharmaceuticals by the US and China, but it seems that the FDA did not update its regulations regarding parabens. FDA considered MP and PP as inactive ingredients when used in pharmaceuticals including analgesics and injection drugs but only 20% of pharmaceuticals included parabens in the US (Soni et al., 2001). On the other hand, a recent study reported that 97% of pharmaceutical products in China contained parabens, with MP being the most common (Ma et al., 2016). These differences between regulations in different countries may result in different levels of water contamination in different world regions since pollution levels reflect consumption and production practices.

3. Parabens occurrence in aquatic environments

Due to their worldwide use, parabens are released into the aquatic environment mainly through domestic wastewater or by the deposition of particles from the atmosphere, resulting in their occurrence in the environment mainly in water sources (Fig. 1). Although their high removal efficiencies (96 to 99.9%) in wastewater treatment plants (WWTP), parabens are still found in surface waters and DW at concentrations ranging from ng/L to μg/L (Wei et al., 2021). This poses a significant risk to aquatic organisms and raises concerns for human health.

3.1. Search method to analyze the occurrence of parabens in water sources

In this specific section, it was crucial to adopt a systematic strategy to analyze and select the data. The data selection was obtained through an advanced search in PubMed and SCOPUS databases, by searching articles using specific keywords (Parabens AND Occurrence AND Water) within Article Title, Abstract and Keywords. This search was done between January 2023 and May 2023. Given the existence of previous reviews on this topic from 1996 until 2012 (Błedzka et al., 2014) and between 2012 and 2020 (Gomes et al., 2020; Wei et al., 2021), the search was limited to articles published between 2020 and 2023. The search returned 38 and 56 articles outputs from PubMed and SCOPUS databases, respectively. From these articles and excluding duplicates, only 34 relevant articles were selected for analysis, along with references from previous reviews (Błedzka et al., 2014; Gomes et al., 2020; Wei et al., 2021). Data regarding the occurrence of parabens in different water sources between 2020 and 2023 are presented as Supplementary information (Tables A1–A3). These studies reported the presence of parabens in water sources mainly in Eastern countries, with only six reports from the EU. Microsoft Excel 16 was used to create World maps graphs (Figs. 2–4) providing an overview of the average maximum concentrations of parabens detected in water sources from publications between 1996 and 2022.

3.2. Parabens occurrence in wastewater

The discharge of parabens-containing PCPs through domestic sewage or garbage is the main source of parabens into WWTP and landfills. WWTP serve as major pathways for paraben release into the environment, especially considering the increasing re-use of treated wastewater globally (Wei et al., 2021). Fig. 2 presents the average maximum concentrations of parabens detected in WWTP influents worldwide between 1996 and 2022, revealing Tunisia as a particularly problematic region with concentrations of parabens exceeding 100,000 ng/L (Haddaoui and Mateo-Sagasta, 2021). This highlights the flexibility for the use of parabens in these countries without limits defined by regulation. Among other parabens, MP was the one detected at the highest concentration of 560,000 ng/L in a Tunisian WWTP influent (Hassine et al., 2011). In the same study, BzP, BP, EP and PP were found at lower concentrations than

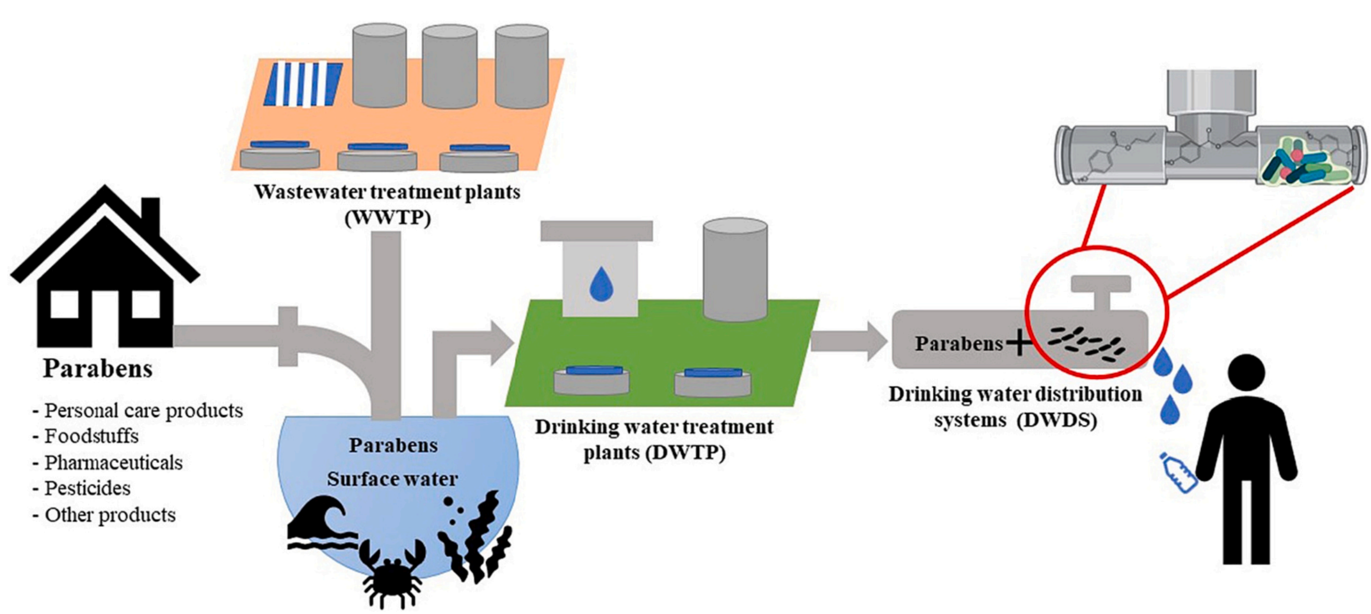

Fig. 1. Schematic representation of the route of parabens into DW point-of-use.

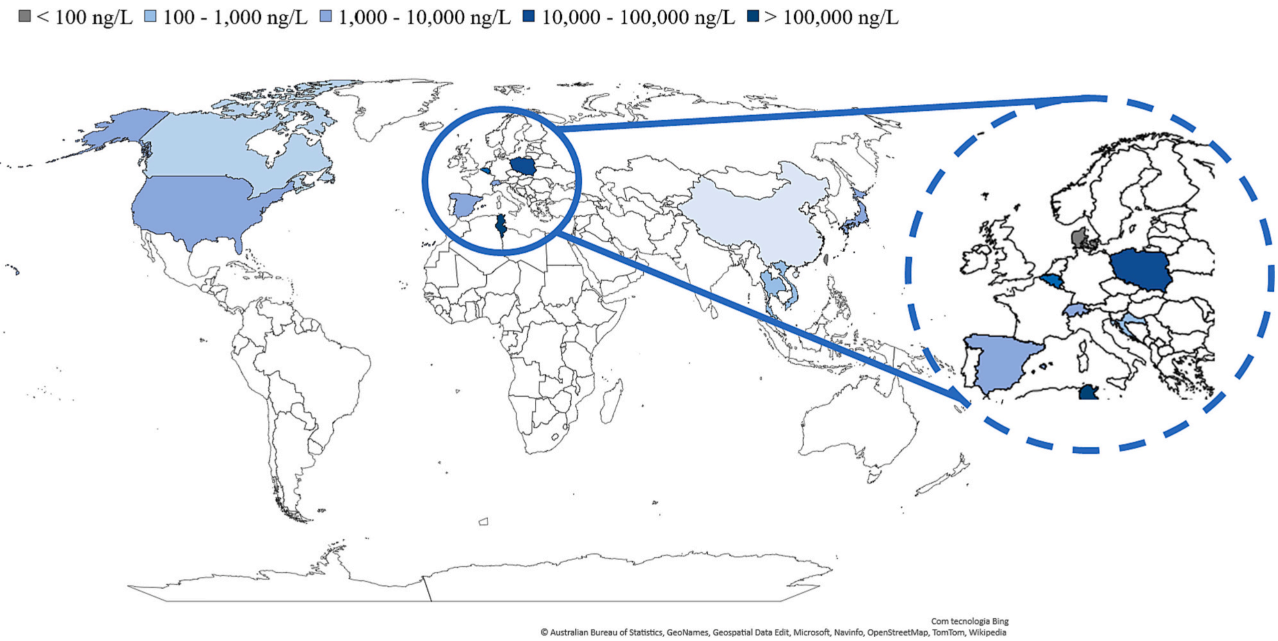

Fig. 2. Average of maximum concentrations (ng/L) detected of parabens in wastewater influents in different countries from 1996 to 2023 (graphical representation developed using Excel plug-in Bing Technology, Australian Bureau of Statistics, GeoNames, Geospatial Data Edit, Microsoft, Navinfo, OpenStreetMap, TomTom, Wikipedia).

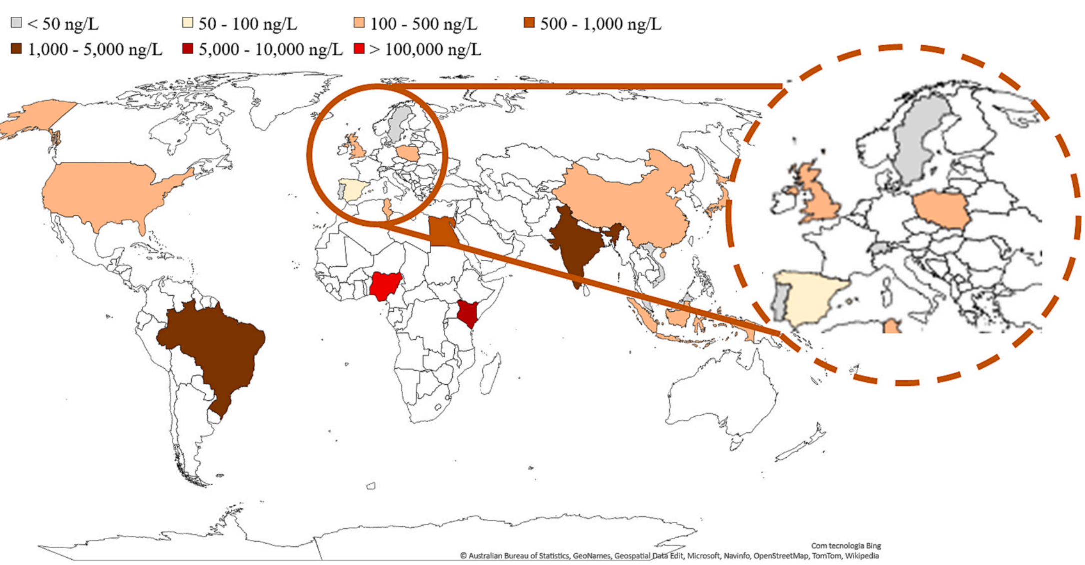

Fig. 3. Average of maximum concentrations (ng/L) detected of parabens in surface waters in different countries from 1996 to 2023 (graphical representation developed using Excel plug-in Bing Technology, Australian Bureau of Statistics, GeoNames, Geospatial Data Edit, Microsoft, Navinfo, OpenStreetMap, TomTom, Wikipedia).

MP, suggesting a higher use of MP in relation to other parabens (Hassine et al., 2011). The concentrations of parabens in WWTP influents are the mirror of societal habits, therefore, regions with greater population density, light regulatory limitation, and industrially active may have higher levels of parabens contamination. In WWTP effluents located in Tunisia and Arabia Saudita, MP was detected at 443000 ng/L followed by PP at 585 ng/L (Haddaoui and Mateo-Sagasta, 2021) (Table A1). Parabens are found in WWTP effluents at lower concentrations than in WWTP influents since these pollutants are expected to be partially removed in WWTP (Wei et al., 2021).

The US also faces significant contamination by parabens, with MP, EP, PP, BP, BzP, and p-HBA being prominent (Fig. 2) (Adhikari et al., 2022). Maximum concentrations of p-HBA (293,000 ng/L) (Wang and Kannan, 2016) and MP (79,600 ng/L) (Błedzka et al., 2014) were reported in New York and Southern California, respectively. Curiously, in Canada, PP was found at a higher concentration (2430 ng/L) than MP (1470 ng/L) (Lee et al., 2005). Despite that, during the severe acute respiratory syndrome coronavirus (2 SARS-CoV-2) pandemic, there was increased consumption of parabens as antimicrobial compounds, as reflected in Arizona's wastewater-based epidemiology data, reflecting consumption intake of these products of 999 ± 102 mg/day per 1000 people (Adhikari et al., 2022).

The presence of parabens in EU WWTP was studied in six countries: Spain (Sadutto et al., 2021; Senta et al., 2022), Switzerland (Jonkers et al., 2009), Poland (Styszko et al., 2021), Belgium and Croatia (Senta et al., 2022), and Denmark (Hayden et al., 2022). The concentrations of

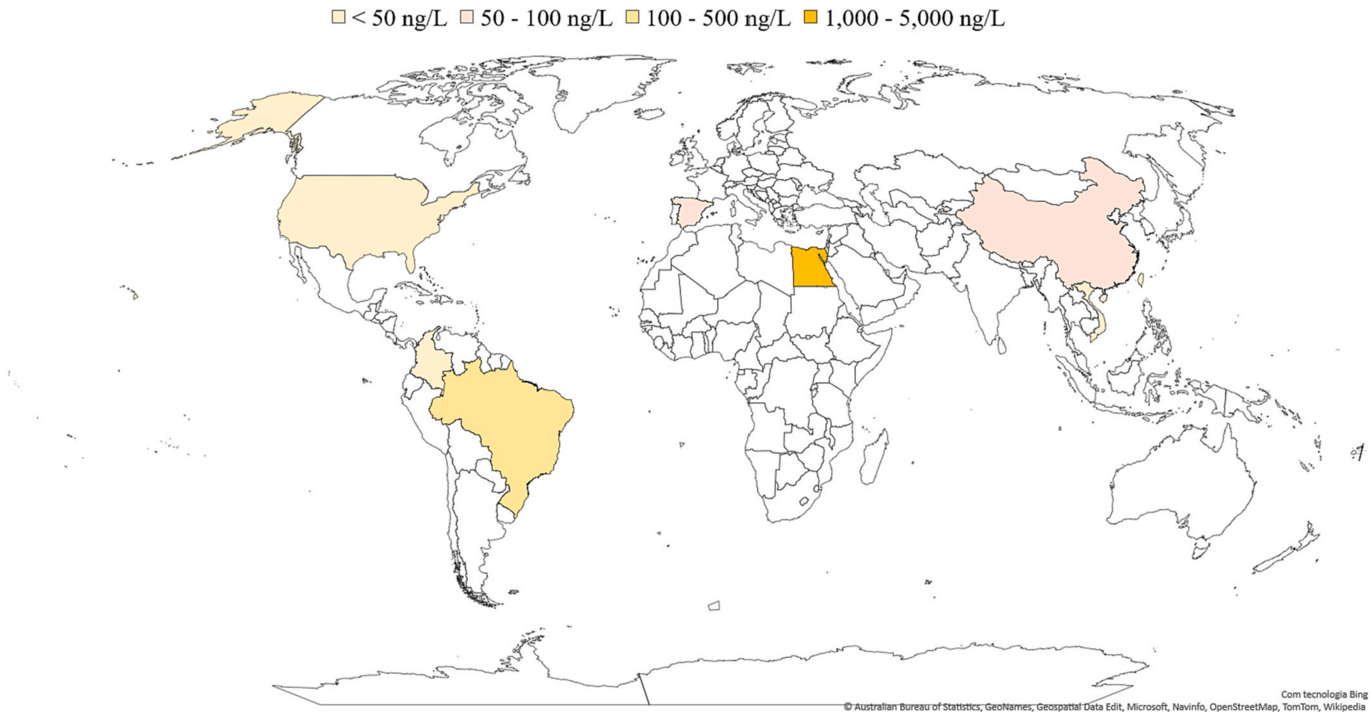

Fig. 4. Average of maximum concentrations (ng/L) detected of parabens in DW in different countries from 1996 to 2023 (graphical representation developed using Excel plug-in Bing Technology, Australian Bureau of Statistics, GeoNames, Geospatial Data Edit, Microsoft, Navinfo, OpenStreetMap, TomTom, Wikipedia).

parabens found were generally lower than those observed in Tunisia, Saudi Arabia, and the US, due to more stringent regulations (Fig. 3). In Croatia and Belgium, MP, EP, PP, and BP were detected in wastewater influents at concentrations ranging from 100 to 1000 ng/L (Senta et al., 2022). In both countries, MP was the paraben detected at higher concentrations (Table A1) (Senta et al., 2022). Spain (Sadutto et al., 2021; Senta et al., 2022), and Switzerland (Jonkers et al., 2009) reported maximum concentrations of parabens in the range of 1000–10,000 ng/L. Recently, in different cities of Spain, namely Valencia (Sadutto et al., 2021) and Girona (Senta et al., 2022), different values of parabens concentrations were found in WWTP influents, with concentrations detected in Girona, reaching values of 2819 and 840 ng/L for MP and PP, respectively. Years before, MP and PP were detected in Santiago de Compostela at higher concentrations: 290–10,000 ng/L for MP and 520–2800 ng/L for PP (González-Mariño et al., 2011). These results suggest not only that MP and PP are the parabens more widely used in Europe, but also that their usage has been decreasing. This may be related to the fulfilment of restrictive regulations in that region. As found in other countries, the concentration and frequency of parabens identified in Spanish WWTP effluents decreased (Derisso et al., 2020). Among different countries in Europe, the presence of parabens in Poland was the most pronounced, being MP detected at 41,000 ng/L in a Polish WWTP influent (Styszko et al., 2021) (Table A1). EP and PP were also found previously in Polish WWTP influents at 4150 ng/L, and 2730 ng/L, respectively (Kapelewska et al., 2018).

Interestingly, Asian countries with high population densities, such as Taiwan, Vietnam, Thailand, and China, exhibited relatively low levels of paraben in WWTP influents (<100–1000 ng/L on average) (Fig. 2). The lowest values detected of MP (179 ng/L), PP (36 ng/L) and EP (2.45 ng/L) were in a WWTP influent in Taiwan (Chen et al., 2020). Among other parabens, in China (Mao et al., 2020) and Vietnam WWTP influents (Le et al., 2022), MP was also the paraben detected at the highest concentration (336.42 and 738 ng/L, respectively). On the other hand, iPP, BP, BzP and heptylparaben (HepP) were found occasionally (Le et al., 2022). Overall, MP was consistently the most commonly detected paraben in WWTP worldwide. This situation was potentiated by the fact of PP and BP being banned and replaced by MP in PCPs (Wei et al., 2021).

3.3. *Parabens occurrence in surface water*

PCPs and other products containing parabens can be directly discharged into surface waters near living areas or released into rivers at residual concentrations from WWTP effluents (Wei et al., 2021). Therefore, surface waters are the most affected by paraben contamination. In Table A2 and Fig. 3, maximum concentrations (ng/L) of parabens detected and reported in surface waters worldwide are presented. Studies have reported the presence of parabens in surface waters across different countries in Africa (Nigeria, Kenya, Egypt, and Tunisia), Asia (Malaysia, China, Japan, India, Indonesia, and Vietnam), America (Brazil, US), and the EU (United Kingdom - UK, Spain, Switzerland, and Sweden).

Africa seems to be the continent more affected by parabens contamination of surface water, revealing the highest values detected (Fig. 3). Nigeria has the highest concentration of parabens reported in surface water, in Osun State (>100,000 ng/L) (Bolujoko et al., 2022). MP was found in Nigerians' surface water at 527,000 ng/L followed by EP at 377,000 ng/L (Bolujoko et al., 2022). In other African countries, MP was also the paraben found at the highest concentration: 10,030 ng/L in Kenya (K'oreje et al., 2022), 1780 ng/L in Egypt (Radwan et al., 2020) and 1048 ng/L in Tunisia (Haddaoui and Mateo-Sagasta, 2021). Those values suggest once again that there is no control over the use of parabens in African countries or specific removal treatments. Moreover, MP is still the paraben most often detected in African surface waters indicating its wide use, which correlates with concentrations found in WWTP. In addition to the presence of parabens in surface waters, these have been also detected in groundwaters in Nigeria (>200 μg/L) (Serra-Roig et al., 2016), Kenya (>70 ng/L) (K'oreje et al., 2022) and Tunisia (>100 ng/L) (Haddaoui and Mateo-Sagasta, 2021). This may occur due to the percolation of parabens into aquifers, uncontrolled hazardous waste release, and rain run-off effect (Serra-Roig et al., 2016).

In America, Brazil reports higher concentrations of parabens (1000–5000 ng/L) (Chaves et al., 2020; Derisso et al., 2020; Reichert et al., 2020) than the US (<500 ng/L) (Fabregat-Safont et al., 2021; Hayden et al., 2022). In Brazilian surface waters, BP was found at the maximum concentration of 11,000 ng/L (Derisso et al., 2020) and EP at the lowest concentration of 5.9 ng/L (Galinaro et al., 2022).

In Asia, India was heavily affected by parabens occurrence (1000 to 5000 ng/L) (Gopal et al., 2021; Kachhawaha et al., 2021; Saha et al., 2022), while China reported concentrations like EU countries (<50–500 ng/L) (Jia et al., 2020; Lu et al., 2022) (Fig. 3). Curiously, Saha et al. (2022) reported that PP was found at higher concentrations (maximum of 8060 ng/L) than MP (maximum of 2979 ng/L) in Indian rivers. However, in other sample points (lakes Ambazari and Khindsi) MP was the paraben detected at the highest concentration (5000 and 18,200 ng/L, respectively), whereas BP was detected at 14,800 ng/L in Nag Niver (Kachhawaha et al., 2021).

Regarding Chinese surface water, Li et al. (2020) reported a higher frequency of detection for iPP (60%) than for MP (20%) in a Chinese river. Moreover, EP was the paraben found at the highest concentration (140 ng/L) in Kitakami River (Japan) followed by BzP, BP and PP with 26, 25 and 24 ng/L, respectively (Gouukon et al., 2020). Therefore, these results suggest that, in Asia, there is no prioritization of using MP in products instead of other parabens.

Poland (Grześkowiak et al., 2016) and the UK (Kasprzyk-Hordern et al., 2009) were the EU countries more affected by parabens contamination in surface waters with concentrations found between 100 and 500 ng/L. This was already expected since Poland was the EU country with higher concentrations of parabens found in WWTP (described in the previous section). MP and PP were the parabens most frequently detected in EU rivers, from 79 to 88%, specifically in Spanish (Sadutto et al., 2021) and Swedish rivers (Malnes et al., 2022). Portugal (Jonkers et al., 2010), Sweden (Malnes et al., 2022; Rehrl et al., 2020) and Switzerland (Jonkers et al., 2009) reported lower concentrations of parabens in surface waters (<50 ng/L) with MP being the dominant paraben (Fig. 3).

3.4. Parabens occurrence in drinking water

The presence of parabens in DW may be due to the incomplete removal of these contaminants in DWTP, as well as the migration of parabens from packaging material (Wei et al., 2021). Since DWTP are the last stage of DW treatment before its distribution and use, the presence of parabens in DW at lower concentrations than those found in WWTP and surface waters is expected. Maximum concentrations of parabens found in DW worldwide including tap water, bottled water, and treated water from DWTP effluents from 2020 to 2023 are presented in Table A3. Fig. 4 shows the average range of maximum concentrations of parabens in DW until date, suggesting a higher contamination in Africa followed by America, EU, and Asia (in descending order). This ranking is in accordance with the one related to the concentrations of parabens reported worldwide in WWTP and surface waters, reflecting the more restricted regulation of the use of parabens in the EU (detailed in Section 2.1).

Although parabens were detected in surface waters and groundwater in Nigeria, the presence of these pollutants in DW was not possible to quantify (<limit of detection - LOD) (Bolujoko et al., 2022). Significant concentrations of MP, PP, and BP in DW reaching maximum values of 1160, 590, and 6380 ng/L, respectively, were reported in Egypt (Radwan et al., 2020).

In America, paraben concentrations in DW in Brazil were higher compared to Colombia and Texas, possibly due to differences in the habits of consumption of products containing parabens, the different treatments used in DWTP, and even due to the disparities in the characteristics of the source waters, resulting in different patterns of environmental contamination by parabens (Fig. 4). While parabens were detected in Brazilian DW samples at concentrations above 100 ng/L [MP - 242 ng/L (Marta-Sanchez et al., 2018); PP - 135.5 ng/L (Caldas et al., 2013)], paraben concentrations below 50 ng/L were found in effluents from DWTP in Colombia (Aristizabal-ciro et al., 2017) and in tap water samples from Texas (Penrose and Cobb, 2023).

To the best of our knowledge, the presence of parabens in EU DW was only explored in Spain, revealing lower concentrations of parabens than those reported in America (except Colombia) and Africa (Fig. 4). Parabens including MP, EP, PP, BP and p-HBA were detected in DW samples from Spain at a maximum concentration of 182.71 ng/L, 4.23 ng/L, 355.89 ng/L (Valcárcel et al., 2018); 28 ng/L (Carmona et al., 2014) and 57 ng/L (Blanco et al., 2009), respectively. The higher values found for MP and PP are in accordance with the fact that those parabens are the most frequently detected in EU surface waters as already described in Section 3.2.

Curiously, Asia was the continent reporting lower concentrations of parabens detected in DW. Parabens (MP, PP, BzP, HepP, and iPP) were found in Asian DW samples, specifically in Taiwan (Pai et al., 2020) and Vietnam (Le et al., 2022) at concentrations below 50 ng/L. However, these studies mainly refer to samples collected from bottled water in supermarkets (1.56–39.9 ng/L) and from tap water directly collected from household faucets (5–54.3 ng/L) (Le et al., 2022).

The present data suggest limited studies registering the presence of parabens in DW. However, since parabens are highly reactive compounds, the formation of disinfection by-products (DBPs) such as halogenated parabens may occur and, therefore, parent parabens are not detected with the same specificity by the available quantification methods. The presence of parabens in DW needs attention, and stricter regulations and control policies in DWTP are necessary to mitigate their occurrence.

3.5. Occurrence of halogenated parabens in water

Chlorination is a common method to control microbial growth in DWDS with sodium hypochlorite being the most frequently used disinfectant (Gackowska et al., 2016). The World Health Organization (WHO) recommends maintaining a residual free chlorine concentration of 0.2 to 0.5 mg/L in treated DW to prevent recontamination by harmful microorganisms (World Health Organization (WHO), 2017). The WHO has set a guideline value of 5 mg/L for total chlorine in DW, considering it safe for lifelong human consumption (World Health Organization (WHO), 2017). However, the presence of phenolic hydroxyl groups in parabens can lead to the formation of halogenated parabens during water disinfection (Fig. 5), becoming a source for human exposure through DW (Penrose and Cobb, 2022).

Studies on halogenated disinfection by-products of parabens began in 2006, showing that typical chlorine levels in tap water can produce chlorinated by-products within a few minutes (Canosa et al., 2006). While halogenated parabens have been usually detected in wastewater, rivers, and swimming pools, their presence in DW was only reported in one study (Penrose and Cobb, 2023) (Table A4). Curiously, metabolites (Ma et al., 2018) and halogenated by-products of parabens (Chen et al., 2020) have been detected in WWTP at higher concentrations than parent parabens.

The US and India have been the most affected by the presence of halogenated parabens, particularly in WWTP (Fig. 6, Table A4). This is expected as these countries have high concentrations of parent parabens detected in WWTP effluents. In fact, 4-hydroxybenzoic acid (4-HB) was detected in a WWTP influent in New York at 293,000 ng/L, followed by 3,4-dihydroxybenzoic acid (3,4-DHB) at 2270 ng/L; methyl protocatechuate (OH-MP) at 346 ng/L and ethyl protocatechuate (OH-EP) at 340 ng/L (Wang and Kannan, 2016). In Indian WWTP, benzoic acid (BA), 4-HB, OH-MP, and OH-EP were detected at 2360, 31,500, 1050 and 392 ng/L, respectively (Karthikraj et al., 2017).

In China, halogenated parabens were also found in WWTP (32.6–32,000 ng/L) (Ma et al., 2018), surface waters (5.05–1625 ng/L) (Li et al., 2016) and even in swimming pools (0.64–1122 ng/L) (Li et al.,

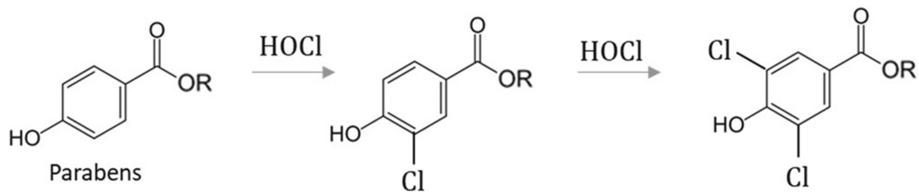

Fig. 5. Formation of halogenated parabens by chlorination disinfection. Created with Chemdraw.

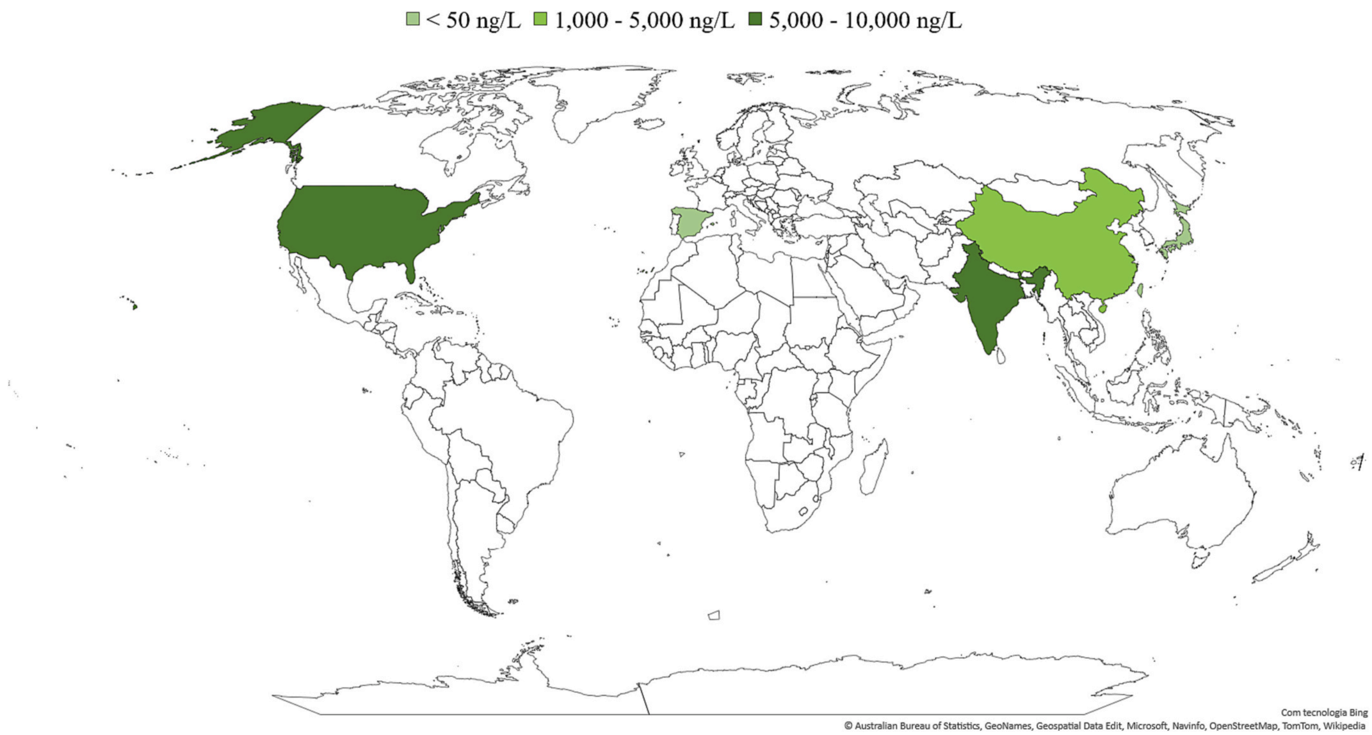

Fig. 6. Average of maximum concentrations (ng/L) detected of halogenated parabens in water sources in different countries over the years (graphical representation developed using Excel plug-in Bing Technology, Australian Bureau of Statistics, GeoNames, Geospatial Data Edit, Microsoft, Navinfo, OpenStreetMap, Tom-Tom, Wikipedia).

2015). The most dominant paraben metabolite observed is p-HBA, but there is no clear trend about the dominant halogenated parabens (Zhao et al., 2022).

Chinese rivers have shown the presence of tri-chlorinated parabens reaching maximum values of 128 ng/L for 3,5-dichloro-4-hydroxybenzoate (3,5-2Cl-EP) (Li et al., 2016). Mono and di-chlorinated parabens were also found in a Taiwan WWTP influent and river reaching values up to 161 ng/L and 11.7 ng/L for di-chlorinated propylparaben (2-Cl-PP), respectively (Chen et al., 2020). While di-brominated benzylparaben (Br_2BzP) was the most often detected (100%), di-brominated butylparaben (Br_2BP) was the one with the greater concentration detected of 110 ng/L in Japanese rivers (Gouukon et al., 2020).

In the EU, chlorinated parabens have only been reported in WWTP influents and effluents in Spain, with di-chlorinated parabens having double the concentration of monochlorinated (González-Mariño et al., 2011).

4. Impact of parabens on human health

A possible route for human exposure to parabens is by the ingestion of contaminated DW. However, the main exposure routes result from the routine use of parabens-containing products. Parabens are absorbed after dermal application as well as after dietary intake or via inhalation (Błedzka et al., 2014). Children and pregnant women are in general more sensitive to parabens than common adults, with higher concentrations found in urine (20–120 μg/L) (Wei et al., 2021). Moreover, the placental transfer efficiency of parabens increases with the increasing of the alkyl chain length (Li et al., 2023). In children's urine samples around the world, MP is highly detected (86%) followed by EP (60%) and PP (60%) (Wei et al., 2021). The maximum concentration of MP detected in children's urine was 79.6 μg/L in Korea (Kang et al., 2013). In Sweden (Larsson et al., 2014), India (Xue et al., 2015b) and China (Lu et al., 2019) this value was below 10 μg/L. The higher content of parabens was observed in older female children (11–14 years old) in comparison with male and younger children (6–10 years old) (Wei et al., 2021). This highlights the different consumption of PCPs containing parabens by different countries and genders. Nevertheless, the general population was also affected by parabens exposure. Overall, people in the US, EU, Japan, and South Korea seem to be exposed to higher levels of parabens than people living in developing countries, which may reflect the higher consumption of these products (Wei et al., 2021). However, in developing countries, strategies to remove parabens from WWTP and even DWTP are not well established, which may help to explain the relatively high concentrations of parabens found in those countries.

The exposure to parabens by humans may lead to some health complications as highlighted in Fig. 7. There are studies reporting parabens' endocrine-disrupting effects mimicking estrogen-like activity and antiandrogenic activity (Lincho et al., 2021). Parabens can bind to the human estrogen-related receptor γ (ERR γ) and disrupt endocrine

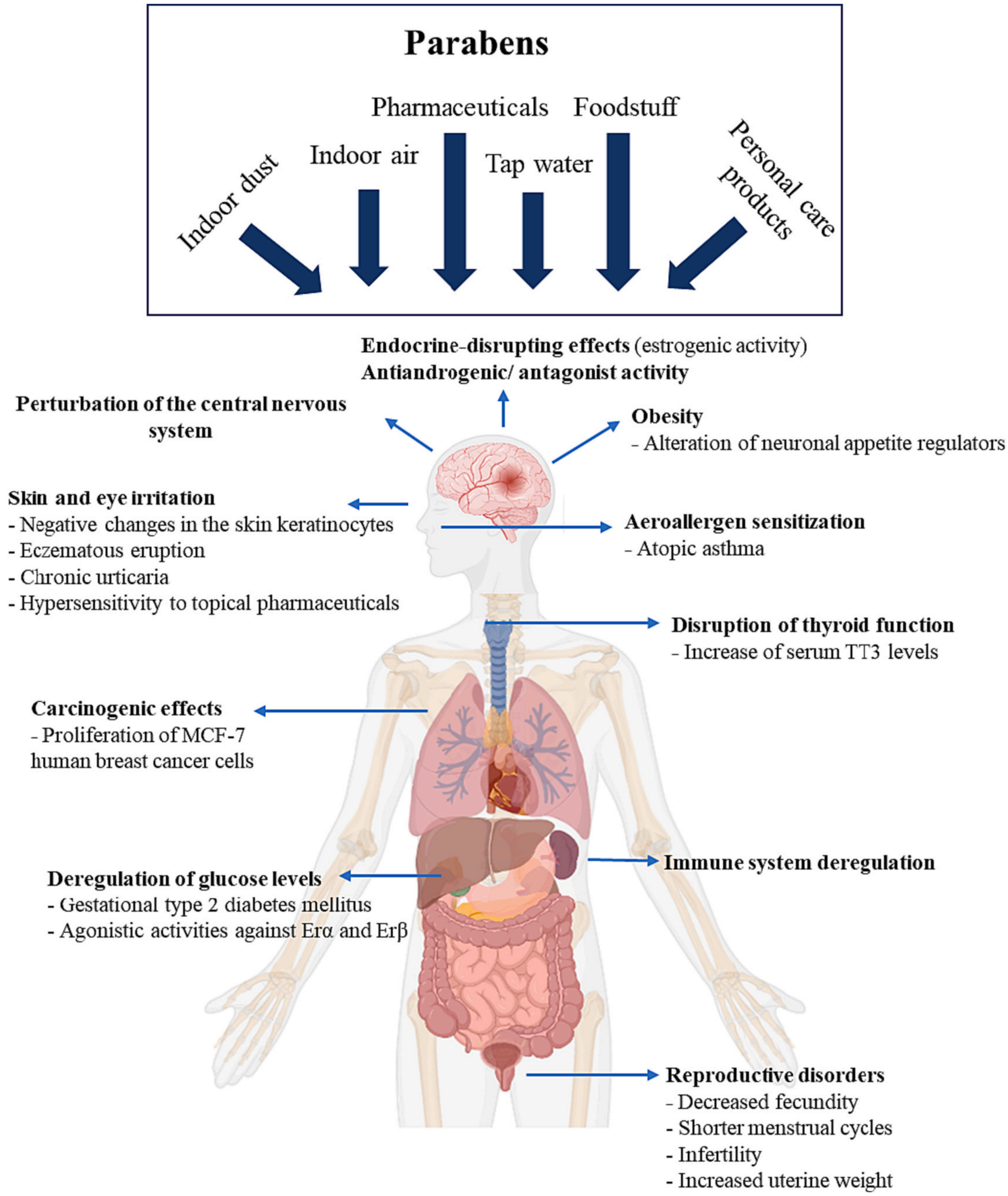

Fig. 7. Parabens human exposure and related health impact. Created with BioRender.com

homeostasis, leading to reproductive disorders and other health complications (Wei et al., 2021). High levels of MP and EP were found in women with reduced fecundity and shorter menstrual cycles (Smarr et al., 2017). Moreover, in another study, PP, BP, and HepP were also associated with reduced female fecundability and highlighted some negative impacts on male sperm count, motility, and quality (Ao et al., 2023).

Parabens are also associated with obesity, and disruption of thyroid function and act as epigenetic modulators causing transgenerational effects (Wei et al., 2021). Moreover, human exposure to parabens (≥180 μg/L) seems to have carcinogenic potential, stimulating the proliferation of MCF-7 human breast cancer cells (Darbre, 2006). Parabens were first detected in human breast tumor tissue in 2004 (Darbre et al., 2004) and median concentrations of 16.8 ng/g of PP, 16.6 ng/g of MP, and 85.5 ng/g for total parabens were found in human breast regions (Barr et al., 2012). Parabens exposure is also associated with DNA damage, an increase in atopic asthma and aeroallergen sensitization, disturbance of the nervous and immune system, lipid homeostasis, distresses in glucose levels (Wei et al., 2021), and skin irritation (Błedzka et al., 2014). Exemplifying, PP causes irritation effects from the application of medicines that contain parabens (Soni et al., 2001), and both MP and PP can cause eye irritation (Soni et al., 2002). Although MP has shown very low toxicity in a wide range of *in vitro* and animal tests, BP induces toxic effects (above 400 mM) against human cell lines (HepG2 and human dermal fibroblasts neonatal) causing a decrease in cell viability by ATP and glutathione depletion (Kizhedath et al., 2019).

Recently, EP was associated with modifications in the systolic blood pressure of patients (Lee et al., 2023). Another recent study also reported that environmental exposure to parabens (EP and PP) was positively correlated to the risk of hypertension (elevated blood pressure levels) and changes in blood pressure (Zhang et al., 2023). This may lead to cardiovascular diseases since high blood pressure is the direct risk factor for cardiovascular diseases and consequently, mortality. Indeed, Yin et al. (2021) reported an association between parabens exposure and cardiovascular diseases. Reimann et al. (2023) found that MP exposure results in increased venular diameter indicating inflammation and atherosclerosis in children, and PP causes a higher retinal tortuosity index, which reflects cumulative vascular damage from hypertension.

Halogenation increases the endocrine-disrupting activity of parent parabens and induces estrogen-antagonistic activity (Penrose and Cobb, 2022). Halogenated parabens act as aryl hydrocarbon receptor (AhR) agonists and induce a broad spectrum of biological responses, including the induction of the cytochrome P450 system, disruption of normal hormone signaling pathways, neuroendocrine, developmental, and reproductive toxicity, immunotoxicity, and mutagenicity (Gouukon et al., 2020).

5. Ecotoxicology of parabens in water sources

Exploring the ecotoxicology of parabens in water sources is essential for interpreting interactions between these ubiquitous chemicals and the ecosystems they permeate. EU legislation classifies hazards to the aquatic environment based on acute and chronic toxicity, bioaccumulation, and degradation of the chemical product (EPA and Homeland Security Research Center, 2011). Acute aquatic toxicity is an intrinsic capacity of a molecule to cause harm to an organism in the short term and is usually expressed using effective concentration (EC_{50}) or lethal concentration (LC_{50}) (Vita et al., 2018). Acute aquatic toxicity tests provide an estimate of the concentration that affects 50% of the population exposed (*i.e.* mortality, inhibition of mobility, interference with reproduction, and reduction in respiration) (Lechuga et al., 2016). Substances are given hazard designations based on LC_{50} or EC_{50} in fish, crustaceans, invertebrates, or algae since these species cover a wide range of aquatic trophic levels (EPA and Homeland Security Research Center, 2011). Chronic aquatic toxicity is an intrinsic capacity of a molecule to cause adverse effects in an organism during aquatic exposure that is determined in relation to the organism's life cycle. For evaluating chronic aquatic toxicity, no-observed-effect concentration (NOEC) and lowest-observed-effect concentration (LOEC) values are used (Vita et al., 2018). The criteria for determining if compounds are toxic to aquatic environments established by the Environmental Protection Agency (EPA) are present in Table 2 (EPA and Homeland Security Research Center, 2011). The toxicity of parabens against aquatic organisms increases as the chain length increases: high EC_{50} and LC_{50} values were associated with MP (being the least acutely toxic) whereas low EC_{50} values were related to BzP (McDonald, 2022). Studies describing the bioaccumulation, biomagnification and toxicity of parabens are described in Sections 5.1 and 5.2.

5.1. Bioaccumulation and biomagnification of parabens on aquatic organisms

Parabens have been found in aquatic life. In Manila Bay (Philippines) MP, PP, and BP were detected in up to 90%, and EP in over 70% of 58 fish samples (Ramaswamy et al., 2011a, 2011b). MP had the highest concentration in fish samples (up to 3600 ng/g) followed by PP (1100 ng/g), EP (840 ng/g) and BP (70 ng/g) (Ramaswamy et al., 2011a, 2011b). Nevertheless, on the other side of the world, parabens were also found in fish samples. In Spanish Mediterranean river basins, BzP, EP, MP, and PP were detected in fish samples at concentrations in the range of 0.35–0.54, 0–0.82, 3.41–84.69, and 0.63–7.43 ng/g, respectively (Pico et al., 2019). Moreover, MP was the predominant compound found in most of the marine mammal tissues analyzed among eight species collected along the coastal waters of Florida, California, Washington, and Alaska (Xue et al., 2015a). The highest concentration of MP detected was 865 ng/g in the livers of dolphins from Sarasota Bay (Xue et al., 2015a). Jeong et al. (2019) found selective accumulation of parabens in certain dolphins' organs, reporting higher concentrations of MP and 4-HB in the kidney, liver, and stomach (Jeong et al., 2019). This was corroborated by Martins et al. (2023) who found higher bioaccumulation of MP in the liver (78.52 ng/g) than in muscle samples (0.01 ng/g) of Brazilian guitarfishes.

A great indicator to assess the bioaccumulation of parabens in organisms' tissues is the bioaccumulation factor, which is defined as the ratio between the concentration of the substance in the tissue and the concentration of the substance in the surrounding environment (Yao et al., 2018). Bioaccumulation factors greater than 1 indicate that the substance is accumulating in the organism's tissues at a higher concentration than in its environment. Martín et al. (2020) reported bioaccumulation factors for parabens in marine animals of 6.47, 4.25 and 3.37 for MP, PP, and EP, respectively. In other animals living near aquatic environments, it was also possible to find high concentrations of parabens and their metabolites accumulated in tissues. MP and 4-HB were found at 796 ng/g in the liver of a bald eagle and 68,600 ng/g in the liver of a white-tailed sea eagle from the Baltic Sea coast (Xue and Kannan, 2016).

Overall, similar to the detection of parabens in aquatic environments, it has been observed that MP exhibit a high accumulation capacity within aquatic organisms, particularly in their liver. Bioaccumulation of parabens (known as endocrine disruptors) in the tissues of organisms can lead to adverse health effects and potentially an advantage for predators in the food chain. Xue et al. (2017) reported the biomagnification of MP in the marine food web consisting of green algae, seagrass species, invertebrates, and mangrove species fished off a US surface water contaminated with MP at a maximum concentration of 31.7 ng/L. In that study, a trophic magnification factor of 1.83 was detected at the higher trophic level (fishes) (Xue et al., 2017). However, Peng et al. (2018) did not corroborate this biomagnification effect revealing only the bioaccumulation of MP and PP in the freshwater fishes, where water was contaminated with MP and PP at maximum concentrations of 15.8 and 21.6 ng/L, respectively.

Biomagnification of parabens occurred when organisms at higher trophic levels tend to accumulate higher concentrations of these pollutants compared to those at lower trophic levels (Xue et al., 2017). Therefore, bioaccumulation and biomagnification of parabens in aquatic organisms may impact humans' health, specifically when these contaminated organisms are ingested overtaking the acceptable daily intake of parabens (10 mg/kg/day) (Ramaswamy et al., 2011a, 2011b).

5.2. Impact of parabens on aquatic organisms

High concentrations of parabens can disrupt the endocrine system of aquatic organisms, affecting animals' reproductive systems and causing animal feminization, abnormal formations, and a decrease in the fecundity of species as found in previous studies (Supplementary information - Table B1) (Lincho et al., 2021). Animal feminization and abnormal formations were observed in *Tigriopus japonicus* (copepods) after exposure to MP, EP and PP (Kang et al., 2019). Reproductive retardations and malformations after parabens exposure were also found in other aquatic organisms such as *Daphnia magna* and *Pimephales promelas* (Dobbins et al., 2009), *Xenopus laevis* (San Segundo et al., 2013), *Drosophila melanogaster* (Chen et al., 2016; Li et al., 2014) and zebrafish (*Danio rerio*) (Dambal et al., 2017; Merola et al., 2020).

Table 2
Criteria for aquatic toxicity (EPA and Homeland Security Research Center, 2011).

	Very high	High	Moderate	Low
Acute aquatic toxicity (LC_{50} or EC_{50} mg/L)	<1.0	1–10	10–100	>100
Chronic aquatic toxicity (NOEC or LOEC mg/L)	<0.1	0.1–1	1–10	>10

Nevertheless, the exposure of aquatic organisms to parabens can also potentiate the increase of oxidative stress biomarkers (Lin et al., 2022) and reactive oxygen species (ROS) (Nagar et al., 2020), lipid peroxidation, and vitellogenin synthesis (Ateş et al., 2018). The increase in vitellogenin by parabens exposure was reported in male fishes such as *Oncorhynchus mykiss* (Alslev et al., 2005); *Oryzias latipes* (Yamamoto et al., 2011); zebrafish (Ateş et al., 2018) and *Cyprinus carpio* (Barse et al., 2010). The inhibition of growth and reproduction (García-Espiñeira et al., 2018) the algae inhibition of photosynthetic efficiency, and diversity decrease are also effects of parabens exposure (Song et al., 2016) as well as coral bleaching (Barbaud and Lafforgue, 2021).

Silva et al. (2018) showed low toxicity of MP revealing 48 h - LC_{50} values 8 times higher than those obtained for BzP against *Oreochromis niloticus* (fish). This lower toxicity of MP among different parabens was also reported against *D. magna* (Lee et al., 2018) and *P. promelas* (Dobbins et al., 2009). Moreover, Lee et al. (2018) reported that toxicity was stronger in the presence of mixed parabens than in single parabens. A mixture of parabens using 10 mg/L of MP, EP, PP, and BzP completely immobilized *D. magna*, caused the mortality of 100% of *Corbicula fluminea* population, slowed down *Raphidocelis subcapitata* and *Lemna minor* growth and decreased the germination index of *Lepidium sativum* (Gomes et al., 2019). Despite the toxicity of parabens against aquatic organisms increases with the increase of the chain length, Nagar et al. (2020) showed values of LC_{50} equal to 78.1 mg/L and 132 mg/L for MP and BP, respectively, being MP more toxic to *Caenorhabditis elegans* (nematode). This highlights the fact that different organisms have different susceptibilities to different parabens (Supplementary information - Table B1).

Bolujoko et al. (2022) suggested that the potential risk of parabens to aquatic organisms is as follows: algae < fish < crustacean. Acute toxicity values (EC_{50}) of parabens vary between 1.20 for BzP and 80 mg/L for MP against algae (*R. subcapitata*), 0.73 for BzP and 63 mg/L for MP against *O. latipes* (fish), and 3.3 to 34 mg/L against crustacean (*D. magna*) for i-BP and MP, respectively (Yamamoto et al., 2011). Moreover, parabens (BP and PP) revealed risk quotients (RQ) > 1 against *D. magna* (Bolujoko et al., 2022). RQ is determined as the ratio between measured environmental concentration (MEC) or predicted environmental concentration (PEC) and the predicted no-effect concentration (PNEC) of the target analyte on the organism (Gopal et al., 2021). Terasaki et al. (2009) reported higher toxicity of parabens (MP, EP, n-PP, i-PP, n-BP, i-BP and BzP) and their chlorinated derivatives against *Aliivibrio fischeri* (bacteria) than *D. magna* (crustacean) with EC_{50} values below 1 mg/L and between 10 and 100 mg/L, respectively. Chlorinated parabens are usually more toxic to aquatic organisms than their corresponding parental parabens (Arfaeinia et al., 2022), corroborating the fact that the toxicity of parabens increases with lipophilicity. Overall, parabens are accumulating in aquatic organisms also due to their lipophilicity (Bilal et al., 2020). Therefore, this characteristic is potentially relevant to the interaction between parabens and microbial communities.

6. Impact of parabens on microorganisms

Although parabens are used as preservatives in several products to prevent the growth of microorganisms (Nowak et al., 2018), the exact mechanism of their antimicrobial effects is not fully understood (Flasiński et al., 2018). Bolujoko et al. (2021) proposed that the mechanism of antimicrobial activity of parabens is linked to the disruption of membrane integrity, leading to leakage of intracellular components (Fig. 8). Parabens can also interfere with bacterial membrane transport processes causing the induction of a potassium efflux (Bredin et al., 2005), or the alteration of the transmembrane potential (Kosová et al., 2015). Other studies suggested that parabens cause the inhibition of DNA, RNA (Fransway et al., 2019), and some vital enzyme synthesis such as ATPase and phosphotransferase (Kosová et al., 2015). Moreover, the respiration of microorganisms may be compromised by parabens since they can inhibit crucial enzymes in the electron transport chain, blocking the flow of electrons, preventing the generation of ATP, and ultimately leading to cell death (Kosová et al., 2015).

The antimicrobial activity of parabens increases with increasing alkyl chain length reporting lower values of minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) (Fransway et al., 2019). Parabens are effective against fungi and bacteria

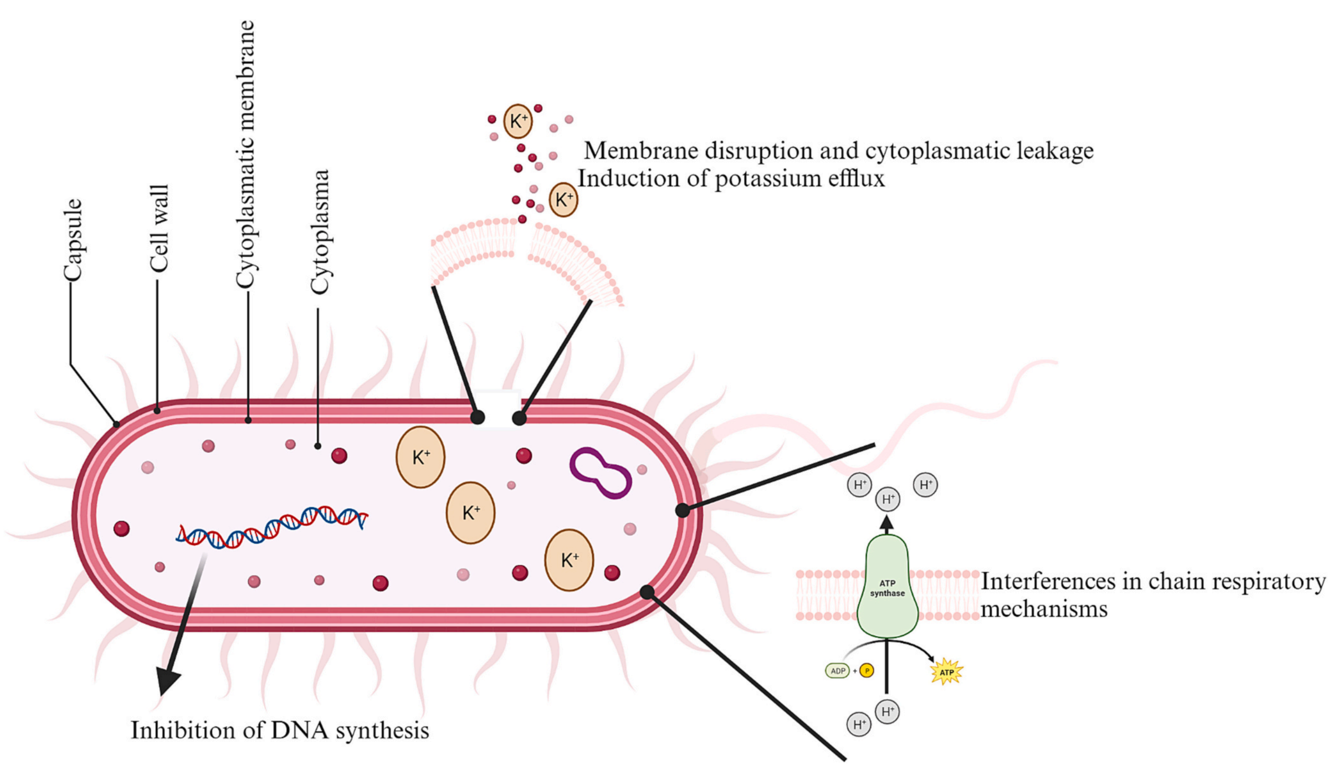

Fig. 8. Schematic representation of the antimicrobial mode of action of parabens. Created with BioRender.com

with stronger antimicrobial properties against fungi, followed by Gram-positive and Gram-negative bacteria (Lincho et al., 2021). Nevertheless, the use of a combination of parabens enhances their antimicrobial activity (Al-Halaseh et al., 2022) as well as if combined with other antimicrobial agents, such as plasma-activated water (PAW) (Liu et al., 2021a, 2021b), UV-A light (Ding and Tikekar, 2020), or nanoparticles (Perni et al., 2015).

Commonly used parabens, in particular MP (Fransway et al., 2019) and EP (Willig et al., 2022) were found to inhibit *Escherichia coli*, *Pseudomonas aeruginosa*, *Aspergillus niger*, *Candida albicans*, *Staphylococcus aureus*, and *Bacillus subtilis*, as reported in Supplementary information (Table C1). However, to achieve this antimicrobial effect, it is necessary to use concentrations around mg/L in parabens formulations, which are higher than those found in aquatic environments (Flasiński et al., 2016).

Although Nagar et al. (2020) reported parabens as toxic to aquatic animals, they found that MP, EP, PP and BP at 1/5 of LC_{50} for *C. elegans* did not cause adverse effects on *E. coli* viability. Moreover, the MBC for PP and BP against *E. coli* was reported to be 100 times above 1/5 of LC_{50} for *C. elegans* (Crovetto et al., 2017). Therefore, the effects of parabens on microorganisms could not be predicted by their toxicity against aquatic organisms. Despite this, other authors showed that the combinations of PP (at 3 mM) and UV-A light (at 2015 $\mu W/cm^2$ or *D*-value of 4.89 ± 0.66 min) for 30 min in aqueous solution (Ding and Tikekar, 2020) or PP (at 4 mM) with plasma-activated water for 10 min (Liu et al., 2021a, 2021b) caused morphological changes in *E. coli*, increased intracellular ROS, and disrupted bacterial membrane potential and integrity. A previous study reported the induction of potassium release in *E. coli* by PP at 0.5 g/L (Bredin et al., 2005). The induction of potassium efflux by PP (at the same concentration of 0.5 g/L) was also detected in *Enterobacter gergoviae* (Davin-Regli et al., 2006). *Streptococcus sobrinus* was also inhibited in the presence of parabens (MP, EP, PP and BP) for 18 h at 37 °C using different concentrations of parabens (Doron et al., 2001). The disruption of the cytoplasmatic membrane and the interference with ATPase were also reported for MP at 0.15% (*w/v*) towards *Listeria innocua* and *P. fluorescens* (Loeffler et al., 2020). Murata et al. (2019) showed that the leakage of internal substances from *Saccharomyces cerevisiae* occurred when combining sulforaphane (1 mmol/L) and MP (0.125 mg/mL).

Flasiński et al. (2018) studied the interaction between parabens (0.001–1 mM) with phospholipidic bacterial and yeast membranes to fill the gap in the interaction between parabens and microorganisms. These authors found that MP, EP, PP and BP induce some surface film modifications affecting the lipid monolayer characteristics, by the measurement of surface pressure (π) – mean molecular area (A) isotherm registration and stability. The alteration of monolayer characteristics by parabens was higher for more hydrophobic parabens, which was reflected in the increased excess area of mixing values (Flasiński et al., 2018). BP strongly affected the bacterial monolayer characteristics, leading to its disruption (Flasiński et al., 2016). The same authors also found that more impactful modifications were detected for Gram-positive bacteria followed by Gram-negative and yeast (Flasiński et al., 2018). Therefore, the impact of parabens on the membranes of microorganisms depends on their chemical structure, solution concentration, and the class of lipids (Flasiński et al., 2016, 2018). Parabens interact more strongly with mammalian membrane components (phosphatidylcholine) than with bacterial membranes (phosphatidylglycerol and cardiolipin), which may explain the cytotoxic activity of parabens (Flasiński et al., 2016).

6.1. Impact of parabens on biofilms

Biofilms are useful tools for assessing the impact of anthropogenic activities on the environment, since microorganisms preferentially adopt surface-associated states, to become more tolerant to environmental stresses when compared to their vulnerable suspended counterparts (Wang et al., 2019a, 2019b). Some authors revealed the antibiofilm properties of parabens, specifically MP against *S. aureus* biofilms (Campbell et al., 2020) and PP and BP against *S. sobrinus* biofilms (Doron et al., 2001). However, the concentrations used are higher than the concentrations typically found in the environment. Therefore, it is important to study the characteristics and behavior of naturally occurring biofilms in the environment exposed to parabens at realistic concentrations to understand their effects on environmental microbiota, in particular, that established in water sources.

Although the interaction between parabens and biofilms is not well understood, it was reported that biofilms may interact with other ECs by different routes (Gomes et al., 2020). Parabens can adsorb onto the biofilm matrix, which can affect their fate in aquatic systems and increase their accumulation (Wang et al., 2019a, 2019b). Some researchers support that this adsorption mechanism can be characterized by the Langmuir model, representing the existence of a monolayer with a finite number of adsorption sites (Viancelli et al., 2020). Environmental aquatic biofilms from rivers and lakes were found to promote the adsorption of pollutants such as phenanthrene, ofloxacin (Wang et al., 2019a, 2019b), miconazole, diclofenac, and carbamazepine (Zhang et al., 2022) or even toxic contaminants like perfluorooctane sulfonate (Bhagwat et al., 2021). This adsorption potentiation seems to be due to changes in surface area and the hydrophobic/hydrophilic characteristics of the samples (Bhagwat et al., 2021). Indeed, chemical modifications of ECs by interaction with EPS-associated functional groups such as (carboxyl, amine, hydroxyl, and phosphoric groups) may occur affecting its hydrophobicity (Hu et al., 2019). Moreover, parabens can interact with the cells within the biofilms, either by adsorption onto the cell wall or by being taken up as nutrients by the biofilm cells (Gomes et al., 2020). Biofilm cells can also release substances that trap these environmental contaminants or facilitate the solubilization of metals (Geng et al., 2019).

Studies evaluating the impact of ECs (including parabens) on environmental biofilms are scarce (Table 3). Most of them reported significant structural and functional modifications in environmental microbial communities after exposure to ECs (mainly antibiotics) (Arruda et al., 2022a; Gomes et al., 2018a, 2018b; Pinto et al., 2023; Wang et al., 2019a, 2019b; Zhang et al., 2021). Among these studies, only five are related to the impact of parabens in environmental biofilms, highlighting their potential ecological consequences (Aristi et al., 2016; Liu et al., 2021a, 2021b; Pereira et al., 2023; Pompei et al., 2022; Yang and Lee, 2023). This low number of studies reflects several limitations and challenges. The complex mixture of ECs (chemical diversity, different modes of action and properties) in the environment is hard to represent and interpret in laboratory assays, representing the main limitation but also the main challenge faced in the available studies (Pereira et al., 2023). In fact, in controlled laboratory conditions, it is hard to replicate the complexity of natural ecosystems and it is difficult to generalize findings across different ECs because they may affect biofilms and planktonic bacteria in unique ways. Nevertheless, quantifying non-pharmaceutical ECs in environmental samples can be technically challenging due to their low concentrations and the need for specialized analytical techniques (Wei et al., 2021). In addition, many of these studies are short-term and may not capture the long-term effects of exposure to parabens (Arruda et al., 2022b).

Regarding biofilms from surface waters, Liu et al. (2021a, 2021b) found that exposure to MP and PP altered the river bacterial community. PP had the highest impact (31.9%) in terms of bacterioplankton community composition variation, followed by MP (21.7%). This variation results from the overexpression of the bacterial genus *Thiovirga* by parabens (MP and PP) (Liu et al., 2021a, 2021b). Moreover, the parabens tested caused the inhibition of Gram-positive bacteria (Firmicutes, Actinobacteria) and promoted oxidative stress-tolerant bacteria in the river ecosystem (Liu et al., 2021a, 2021b). Other authors found increased antibiotic resistance of microbial community in freshwater rivers and sediments after exposure for 15 weeks to parabens (MP, EP, PP, and BP at 90 μg/mL) and modifications in the nitrogen and sulfur

Table 3
Impact of ECs (pharmaceuticals, musks and parabens) on environmental biofilms and planktonic bacteria.

Class of ECs	ECs	Type of assay	Effects	References
Pharmaceuticals	Macrolides, quinolones, sulfanamides, tetracyclines and chemotherapeutic	Mediterranean river (Artificial streams)	- Change in the bacterial community: α-Proteobacteria and Acinetobacteria were more abundant in biofilms - Increase in mortality - Decreased extracellular peptidase and phosphatase	(Proia et al., 2013)
	Cimetidine (0.015 M)	Stream biofilms	- 51% biofilm respiration reduction - 4% algal biomass reduction	(Rosi-Marshall et al., 2013)
	Ciprofloxacin (0.013 M)		- 91% biofilm respiration reduction - 22% algal biomass reduction	
	Di-phenhydramine (0.13 M)		- 63% biofilm respiration reduction - 99% photosynthesis inhibition - Shift in the bacterial community (increased *Pseudomonas* sp. and decreased of *Flavobacterium* sp.)	
	Mixed combination: Caffeine + Cimetidine + Ciprofloxacin + Diphenhydramine + Metformin + Ranitidine (0.012–0.015 M)		- 18% algal biomass reduction - 40% biofilm respiration reduction - 88% photosynthesis inhibition	
	Carbamazepine, Sulfamethoxazole, Erythromycin, Metoprolol, Atenolol, Ibuprofen, Diclofenac, Gemfibrozil, Hydrochlorothiazide		- Increased metabolic activity - Reduction of the operational taxonomic units richness	(Corcoll et al., 2015)
	Sulfadiazine and sulfathiazole	*Fusobacteria* in rivers	- Increased ARGs expression (bla_d gene) - Increased reproduction	(Qiu et al., 2019)
	Antibiotic residues	Facultative pathogenic bacteria biofilms in influents and effluents of WWTP in Southern Germany	- Occurrence of antibiotic-resistant bacteria - Antibiotic resistance genes (ARGs) blaTEM, ermB, tetM, sul1, mecA, blaCMY-2, blaKPC-3 and mcr-1 - Multidrug resistance	(Reichert et al., 2021)
	Tetracycline (1000 μg/L), sulfadiazine (1000 μg/L) and chloramphenicol (1000 μg/L) Mixed combination:333 μg/L each	Biofilm bacterial community (*E. coli*) on simulated DW supply pipe wall	- Promotion of the growth of bacteria in biofilm - Enhanced the bacterial chlorine resistance in the effluent, but reduced that in the biofilm - Reduction of the richness of biofilm communities	(Zhang et al., 2021)
	Ciprofloxacin (2 μg/L), Sulfadiazine (2 μg/L)	Multi-species biofilm from DW	- Increased total bacteria in biofilms - Increased *Hyphomicrobium* - Decreased *Sphingopyxis* - Increased *mexA* - Increased ciprofloxacin resistance genes (*qnrB and qnrS)* - Increased sulfadiazine resistance genes (sul1, sul2 and sul3) - Increased proteases and dehydrogenases production	(Wang et al., 2019a, 2019b)
	Ciprofloxacin (1 μg/L) + Sulfadiazine (1 μg/L)		- Increased total bacteria in biofilms - Increased *Hyphomicrobium* - Decreased *Sphingopyxis* - Increased *mexA* - Increased ciprofloxacin resistance genes (*qnrB and qnrS)* - Increased sulfadiazine resistance genes (sul1, sul2 and sul3) - Increased proteases and dehydrogenases production - Increased proteins content in biofilm EPS	
	Carbamazepine (586 ng/L), ciprofloxacin (679.7 ng/L), ibuprofen (223.6 ng/L)	*A. calcoaceticus* biofilms from DW	- Ibuprofen exposure decreased biofilm formation ability by 11%, while MIX exposure increased it by 16%. - Carbamazepine and ciprofloxacin exposures increased susceptibility to trimethoprim-sulfamethoxazole - Ciprofloxacin and ibuprofen increased tolerance to NaOCl - Carbamazepine decreased tolerance to NaOCl - Ciprofloxacin increased *A. calcoaceticus* growth rates	(Pinto et al., 2023)
	Carbamazepine (258 ng/L and 258,000)	Planktonic and biofilm tests with *B. cepacia* from DW	- Increased biofilm susceptibility to sodium hypochlorite at 5 mg/L	(Gomes et al., 2019a)
	Antipyrine (400 ng/L and 400,000)		- Increased tolerance of planktonic cells to chlorine (increase MBC)	
	Diclofenac (6 ng/L and 600 ng/L)		- Increased tolerance of planktonic cells to chlorine (increase MBC) - 13% of swarming motility increase	
	Trimethoprim (1.7 ng/L and 170 ng/L) Sulfamethoxazole (8.2 ng/L and 820 ng/L)		- Increased biofilm susceptibility to sodium hypochlorite at 5 mg/L - Increased tolerance of planktonic cells to chlorine (increase MBC)	

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Table 3 (*continued*)

Class of ECs	ECs	Type of assay	Effects	References
			- 14% of swarming motility decrease	
	Clofibric acid (170 ng/L), Carbamazepine (258 ng/L)	*S. maltophilia* biofilms from DW	- Increased biofilm susceptibility to sodium hypochlorite at 130 mg/L	(Gomes et al., 2018a, 2018b)
	Clofibric acid (17,000 ng/L), Carbamazepine (25,800 ng/L), Ibuprofen (300 ng/L)		- Increased biofilm susceptibility to sodium hypochlorite at 130 mg/L - Exposed bacteria formed lower amount of biofilm than non-exposed bacteria	
	Diclofenac (600 ng/L), Ibuprofen (300 ng/L), Tylosin (170 ng/L)		- Increased biofilm proliferation	
	Clofibric acid (170 and 17,000 ng/L)		- Increased biofilm tolerance to sodium hypochlorite - Increased biofilm tolerance to erythromycin - Reduction of the ability of *S. maltophilia* to invade HT29 human cell line	(Gomes et al., 2019b)
Musk fragrance	Galaxolide (2.2 ng/L and 220 ng/L)	Planktonic *B. cepacia* from DW	- 12% of swarming motility increase	(Gomes et al., 2019a)
	Tonalide 150 ng/L	Mixed biofilms: *A. calcoaceticus*, *B. cepacia* and *S. maltophilia* from DW	- Increased cellular culturability, viability and density - Increased EPS content of biofilms on SS316 - Increased ability to form new mixed biofilms - Increased biofilm tolerance to chlorine	(Arruda et al., 2022a, 2022b)
		S. maltophilia from DW	- Decreased culturability	
		B. cepacia from DW	- Increased swarming motility	
		A. calcoaceticus from DW	- Increased swimming motility	
	Galaxolide 150 ng/L	Mixed biofilms: *A. calcoaceticus*, *B. cepacia* and *S. maltophilia* from DW	- Increased culturability on PVC	
		A. calcoaceticus from DW	- Decreased the cellular density on PVC - Increased ability to form biofilms on PVC - Increased susceptibility to chlorine - Increased swimming motility	
		S. maltophilia from DW	- Increased viability - Increased susceptibility to chlorine - Increased swimming motility	
		B. cepacia from DW	- Increased susceptibility to chlorine	
Pharmaceuticals + Preservatives	Mixed combination: Ciprofloxacin, Erythromycin, Sulfamethoxazole, Diclofenac (1 μg/L) + MP (0.1 μg/L)	Artificial stream Llémena River (Spain)	- Weak toxic effects after 3–4 weeks of exposure - 10% community respiration reduction - Decreased of basal fluorescence	(Aristi et al., 2016)
	Mixed combination: Ciprofloxacin, Erythromycin, Sulfamethoxazole, Diclofenac (1 μg/L) + MP (0.1 μg/L)	Stream biofilms	- Increased bacteria resistance - Reduction of algal biomass - Reduction of taxa richness - Increased biofilm metabolic rates - Increased number of unicellular green algae	(Subirats et al., 2018)
	Mixed combination: Paracetamol, Diclofenac, Naproxen, Ibuprofen, MP, Benzophenone-3 (2 μg/L)	Algae and cyanobacteria communities in ecological filters during DW treatment	- Changes in the composition of algae and cyanobacteria community	(Pompei et al., 2022)
Preservatives	MP, PP (>61.6 ng/L)	Bacterioplankton community in urban rivers in China	- Bacterioplankton community changes by PP (31.9%) and MP (21.7%) - Promoted oxidative stress-tolerant bacteria	(Liu et al., 2021a)
	MP, EP, PP and BP (at 90 μg/mL for each paraben)	Microbial community in freshwater river water and sediments	- After 15 weeks of exposure: increase in tetracycline-, sulfamethoxazole- and paraben-resistant microbes and xenobiotic-degrading microbes - Modifications in the nitrogen and sulfur cycles	(Yang and Lee, 2023)
	Triclosan (60 μg/L)	River biofilms (artificial streams)	- Increase in mortality - Recovery of biofilm - Reduction of the phosphorous uptake rate	(Proia et al., 2011)
	Triclosan (12 mg/L)	Artificial streams	- Increased resistance of bacteria to triclosan - Decreased stream community diversity - Shift in bacterial community composition	(Drury et al., 2013)
	MP, PP, BP, and a triple combination of all (MIX) (150 ng/L each)	*A. calcoaceticus* biofilms from DW *S. maltophilia* biofilms from DW	- Increased bacterial culturability and density - MP: increased biofilm thickness and changes on biofilm conformation; increased polysaccharides content; increased swimming motility and virulence factors production of *S. maltophilia* bacteria from *S. maltophilia* biofilms	(Pereira et al., 2023)
	MP (150 ng/L)	Dual-species biofilms composed by *A. calcoaceticus* and *S. maltophilia*	- Increased bacterial membrane damage - Increased biofilm thickness - Modification of biofilm conformation	
Pesticide	Diuron (15 μg/L)	River biofilms (artificial streams)	- Increase in mortality - Decreased photosynthetic efficiency - Increase of extracellular enzymes/cell activity (alkaline phosphatase and leucine aminopeptidase) - Recovery of biofilm	(Proia et al., 2011)
Central nervous systems stimulant	Amphetamine	Artificial streams	- Decreased biofilm chlorophylla production and respiration	(Lee et al., 2016)

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Table 3 (*continued*)

Class of ECs	ECs	Type of assay	Effects	References
Neuroactive stimulant	Caffeine (119 ng/L and 11,900 ng/L)	Planktonic *B. cepacia* from DW	- Shift of microbiota: increase of *Cloacibacterium* spp., *Coconeis placentula* and *Reimeria uniseriate* and decrease of *Luteimonas* spp. - Increased tolerance of planktonic cells to chlorine (increase MBC) - 10% of swarming motility decrease	(Gomes et al., 2019a)
	Caffeine (158.7 ng/L)	*A. calcoaceticus* biofilms from DW	- Decreased susceptibility to trimethoprim-sulfamethoxazole	(Pinto et al., 2023)
	Caffeine (0.015 M)	Stream biofilms	- 22% algal biomass reduction - 53% biofilm respiration reduction	(Rosi-Marshall et al., 2013)

Legend: *A. calcoaceticus* - *Acinetobacter calcoaceticus*; *B. cepacia* - *Burkholderia cepacia*; DW - drinking water; EPS - extracellular polymeric substances; MP - methylparaben; MBC - minimum bactericidal concentration; PCPs - personal care products; PVC - polyvinyl chloride; *S. aureus* - *Staphylococcus aureus*; *S. maltophilia* –*Stenotrophomonas maltophilia*; SS316 - stainless steel AISI 316.

cycles (Yang and Lee, 2023). Different stream biofilm samples, exposed to a combination of pharmaceuticals (ciprofloxacin, erythromycin, sulfamethoxazole, diclofenac) at 1 μg/L and MP at 0.1 μg/L were affected in the reduction of respiration and a decrease in the basal fluorescence of biofilms (Aristi et al., 2016), as well as reduction of algal biomass and taxa richness (Subirats et al., 2018). Contrarily, Pompei et al. (2022) reported an increase in the diversity of algae and cyanobacteria biofilms formed on filters during the treatment of DW and exposure to a combination containing pharmaceuticals and MP at 2 μg/L, suggesting that exposure to these contaminants may favor the proliferation of these photosynthetic microorganisms.

More worrisome is the alteration verified on biofilms formed by bacteria isolated from DW sources in the presence of parabens. Recently, Pereira et al. (2023) found that *Stenotrophomonas maltophilia* and *Acinetobacter calcoaceticus* biofilms grown in the presence of trace concentrations (150 ng/L) of MP, PP, BP, and a triple combination had increased bacterial cell culturability and cell density. MP was the paraben that caused more pronounced modifications on the biofilm cells, also affecting the membrane integrity of bacteria as well as biofilm thickness and structural conformation (Pereira et al., 2023). Moreover, MP exposure promoted an increase in virulence factor production by *S. maltophilia* from biofilms. In that study, dual-species biofilms were also affected by the presence of MP, revealing increased biofilm thickness and significant modifications in the biofilm conformation (Pereira et al., 2023). These changes in biofilm behavior may impact the quality of DW delivered through plumbing systems, highlighting the need to prioritize the control of parabens in these systems.

6.2. *The effect of parabens on the tolerance to antimicrobials*

The overuse of antibiotics and other chemicals in various fields such as human and animal health, agriculture and aquaculture, has led to the emergence and spread of antibiotic resistance. This resistance poses a significant challenge as it contaminates food and water sources, making infections harder to treat (Ma et al., 2019). Therefore, antibiotic-resistant bacteria (ARBs) and genes (ARGs) in the environment have become considered pollutants of emerging concern, being commonly found in WWTP, which favors the transmission of antimicrobial resistance into other water sources and the possible transmission of resistant strains to humans and animals (Guruge et al., 2021). Xi et al. (2009) found that the prevalence of ARGs was higher in tap water (consumption point) than in source (DWDS influents) and finished water (DWDS effluents). The same author also showed that the levels of ARBs were higher in tap water than in finished water, suggesting that regrowth of bacteria in DW plumbing systems occurs (Xi et al., 2009). In household DW samples collected in China, among 265 ARG, *bacA* (bacitracin) and *mexF* (multidrug) were the most detected genes (Ma et al., 2019). Moreover, resistant phenotypes to ceftazidime and meropenem were found in isolates from DWTP in the North of Portugal (Figueira et al., 2011). Biofilms from DWTP showed also to be a reservoir of class 1 integrons (associated with multidrug resistance) (Farkas et al., 2013).

The influence of the extensive use of parabens on the dissemination of resistance determinants is not yet fully understood (Stanton et al., 2022). However, other authors propose that the uncontrolled use of PCPs containing parabens can contribute to the spread of antimicrobial resistance (Caioni et al., 2023).

Bacterial resistance mechanisms to parabens are like those of other antimicrobials involving efflux pumps, cell wall and membrane modifications (Flasiński et al., 2018), enzyme expression, stress response pathways (Bolujoko et al., 2021) and gene promotion encoding resistance to antibiotics (Fahimipour et al., 2018). Resistance to parabens has been reported in *P. aeruginosa*, *B. cepacia*, and *Cladosporium resinae* (Valkova et al., 2001). Fahimipour et al. (2018) showed that although parabens (BzP, PP, MP, BP, and EP at concentrations from 1.6 to 352 ng/g of dust) did not potentiate antimicrobial resistance in indoor microbial communities, exposure to triclosan and triclocarban (which are also preservatives often used in PCPs) increased the number of cross-resistant bacteria to clarithromycin, ampicillin, and tetracycline. This suggests a lower impact of parabens on antimicrobial resistance in comparison to antibiotics. Contrarily, Hartmann et al. (2016) found that the presence of ARGs (*cmr* efflux pump, *erm*(33) and *erm*(C)) in the indoor dust microbiome was associated with high concentrations of MP at 320–1470 ng/g dust. Moreover, the exposure to PP at 0.5 mg/mL also induced potassium efflux in *E. coli* (as a mechanism of resistance), which was accelerated by the presence of a functional outer membrane protein (OmpF - a porin) (Bredin et al., 2005). A recent study evaluated the impact of MP, EP, PP and BP (at 90 μg/mL for each paraben) for 15 weeks on microbial community resistance in freshwater river water and sediments and found an increase in tetracycline-, sulfamethoxazole- and paraben-resistant microbes and xenobiotic-degrading microbes (Yang and Lee, 2023). Curiously, the effects of parabens on antibiotic resistance were more pronounced for MP followed by EP, PP and BP, which is stronger for parabens with smaller allylic chains (more hydrophilic). When combining 0.1 μg/L of MP with ciprofloxacin, erythromycin, sulfamethoxazole, diclofenac at a constant concentration of 1 mg/L, the increase in the resistance to sulfonamides (*sul1* and *sul2* genes) and *intI1* gene was found in biofilm streams (Subirats et al., 2018), which may indicate that the presence of parabens promotes antimicrobial resistance by the increase of ARG.

Other classes of ECs, mainly antibiotics, have also been described as potential contributors to the spread of resistance in the environment (including in water environments) (Gomes et al., 2019a; Pinto et al., 2023; Wang et al., 2019a, 2019b, 2023). Therefore, since the use of parabens is associated with a possible enhancement of antibiotic resistance, it is also important to assess whether the use of parabens hinders water disinfection processes. Unfortunately, even after water disinfection treatments, the existence of chlorine-resistant bacteria surviving in DWDS still occurs and may carry an additional risk of antibiotic resistance (Khan et al., 2016). In these cases, chlorination may promote the conjugative transfer of ARGs by increasing cell permeability (Sharma et al., 2016) and can increase the expression of multidrug efflux pumps (Xi et al., 2009). For example, Shi et al. (2013) found that DW chlorination using sub-inhibitory concentrations increased surviving *Proteobacteria* resistant to chloramphenicol, trimethoprim and cephalothin, and enhanced genes encoding resistance to β-lactams (*blaTEM-1*; *ampC*), tetracycline (*tetA*; *tetG*), aminoglycoside (*aphA2*), and erythromycin (*ermA*; *ermB*). However, there are no works evaluating the effects of parabens on compromising water disinfection. To the best of our knowledge, there are only five reports evaluating the effects of other ECs (mainly antibiotics and musk fragrances) on DW bacterial susceptibility to chlorine and none of them include parabens (Arruda et al., 2022a; Gomes et al., 2018a, 2019a, 2019b; Pinto et al., 2023). These studies reported some changes in DW bacterial community susceptibility to chlorine disinfection (Table 3). However, different conclusions were obtained, dependent on the pollutant tested, bacterial model, and time of exposure, which does not allow to predict the effects of other ECs, nor the real effects of the presence of combinations of pollutants in water disinfection.

7. Conclusions

Parabens have long been taught to have minimal toxicity and an excellent safety record being widely used in daily routine products. However, recent concerns have emerged due to their observed endocrine-disrupting activity, as well as their widespread environmental dissemination, particularly in aquatic systems. This review underscores that parabens are consistently worldwide detected in DW at trace concentrations ranging from 3 ng/L to 6 μg/L, being MP the most often detected. The same tendency also occurs in WWTP and surface waters but at higher concentrations (>100 μg/L). The distribution of parabens in water sources appears closely associated with the regulation applied by each country for the use of parabens, as well as with the water treatment strategies implemented. Pristine parabens were found to interfere with hormonal synthesis and impact the growth and development of aquatic organisms. However, more worrying than parent parabens is the generation of chlorinated parabens resulting from chlorine-based water disinfection processes. These chlorinated parabens seem to have higher ecotoxicity and pose increased risks to animal and human health. The interaction between parabens and microbial communities (mainly in aquatic environments) is now documented, providing scientific evidence of changes in microbial structure, biodiversity, and alterations in bacterial behavior. These alterations influence biofilm tolerance to chlorine and antibiotics, with a more pronounced impact on Gram-positive bacteria with a significant disturbance of the bacterial membrane. When a biofilm is exposed to parabens, these seem to adsorb into the sessile structure, but the effects on antimicrobial tolerance are controversial, highlighting that further research is needed to understand how parabens can interfere with the action of an antimicrobial molecule. Further limitations on the scientific understanding of the impact of parabens in aquatic systems are related to the need of accurate and advanced techniques for the identification and quantification of parabens and derivatives at the environmental concentrations, and the absence of comprehensive and long-term studies in the environmental settings or under realism-based conditions.

CRediT authorship contribution statement

Ana Rita Pereira: Conceptualization, Methodology, Investigation, Data curation, Writing – original draft. **Inês B. Gomes:** Conceptualization, Writing – review & editing, Supervision. **Manuel Simões:** Conceptualization, Resources, Writing – review & editing, Supervision, Project administration, Funding acquisition.

Declaration of competing interest

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

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

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