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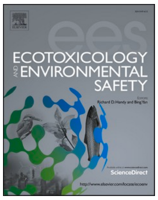

Environmental impacts, exposure pathways, and health effects of PFOA and PFOS

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ABSTRACT

Per- and polyfluoroalkyl substances (PFAS) are synthetic chemicals that have been widely utilized in various industries since the 1940s, and have now emerged as environmental contaminants. In recent years, perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) have been restricted and replaced with several alternatives. The high persistence, bioaccumulation, and toxicity of these substances have contributed to their emergence as environmental contaminants, and several aspects of their behavior remain largely unknown and require further investigation. The trace level of PFAS makes the development of a monitoring database challenging. Additionally, the potential health issues associated with PFAS are not yet fully understood due to ongoing research and inadequate evidence (experimental and epidemiological studies), especially with regard to the combined effects of exposure to PFAS mixtures and human health risks from drinking water consumption. This in-depth review offers unprecedented insights into the exposure pathways and toxicological impacts of PFAS, addressing critical knowledge gaps in their behaviors and health implications. It presents a comprehensive NABC—Needs, Approach, Benefits, and Challenges—analysis to guide future strategies for the sustainable monitoring and management of these pervasive environmental contaminants.

1. Introduction

Industrialization and urbanization have caused environmental degradation through the pollution of emerging organic contaminants, with the global contamination crisis not only being subjected to anthropogenic stressors but also naturogenic influences such as seasonality, climate change, natural disasters, and geological, atmospheric, and hydrological factors. Per- and polyfluoroalkyl substances (PFAS) are a diverse group of synthetic chemicals that have been widely used in industrial applications and in the production of consumer goods for more than 80 years, owing to their resistance to grease, oil, water, and heat, including their use in chemical, electronic, photographic, military, aviation, agricultural, packaging, and textile applications (Hu et al., 2016; OECD, 2018; Post et al., 2012; Wang et al., 2017). While there are thousands of different PFAS, only a few are being monitored and have regulatory concerns, such as perfluorooctanoic acid (PFOA), perfluorooctane sulfonate (PFOS), perfluorohexane sulfonate (PFHxS), perfluoroheptanoic acid (PFHpA), perfluorononanoic acid (PFNA), and perfluorodecanoic acid (PFDA) (Sunderland et al., 2019).

PFOA and PFOS are the most detected and explored PFAS in the global environment, and although they have been restricted in recent years, several alternatives have increased substantially (Fig. 1). Ongoing research and monitoring, health effects, treatment technology, and regulation remain limited to PFOA and PFOS, with several characteristics, factors, modes, and mechanisms yet to be investigated, including persistence, accumulation in animals, humans, and the environment, exposure in a variety of ways, and potential ecological and human health effects continue to pose concerns (OECD, 2022; US EPA, 2022a). These compounds are commonly detected in riverine, estuarine, and marine ecosystems and are closely linked to the anthroposphere and hydrological cycles. Their entry into the food chain, food web, and water system has resulted in their presence in food and water supplies, leading to chemical risks via dietary exposure. In November 2016, the Food and Drug Administration (FDA) abolished the use of long-chain PFAS, including PFOA and PFOS, in food contact applications in the United States. Additionally, the Centers for Disease Control and Prevention's

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(CDC) Agency for Toxic Substances and Disease Registry (ATSDR) is currently investigating human exposure and the health effects of PFAS through drinking water consumption. In 2018, the ATSDR proposed drinking water levels of 11 ng/L and 7 ng/L for PFOA and PFOS, respectively. In 2022, the United States Environmental Protection Agency (US EPA) recommended stricter standards for PFAS in drinking water, with revised limits of 0.004 ng/L for PFOA and 0.02 ng/L for PFOS, down from the previous 70 ng/L lifetime drinking water health advisory level set in 2016 (US EPA, 2022b). Thereafter, a new National Primary Drinking Water Regulation proposed an enforceable maximum contaminant level of 4 ng/L for PFOA and PFOS in drinking water in March 2023 (US EPA, 2023). Chemical risk due to dietary exposure via drinking water has arisen from arsenic, fluoride, or nitrate to emerging contaminants, particularly PFAS (WHO, 2022).

Developed countries are often at the forefront of developing and enforcing stringent guidelines for emerging contaminants, such as PFAS (ITRC, 2022). However, in many developing and underdeveloped countries, PFAS regulations are not yet common. Standards in these countries are often limited to physical parameters (pH and turbidity), chemicals (disinfectants, disinfection by-products, nutrients, metals, and major ions; organic chemicals include only pesticides, petroleum products, and solvents), microbiological properties (coliforms and *Escherichia* coli), and organoleptic characteristics (taste, odor, and color). Examples of such standards include the National Water Quality Standards for Malaysia, Indian Standards for Safe Drinking Water, Philippine Clean Water Act, Chinese National Quality Standards for Drinking Water and Surface Water, Turkish Water Pollution Control Regulation, Bangladesh Environment Conservation Act, South African Water Quality Guidelines, and United Arab Emirates' Water Quality Regulations. Unfortunately, individuals and populations are still exposed to PFAS due to their occurrence and dispersion in the global water environment (surface water, groundwater, and drinking water), including in Africa (Essumang et al., 2017; Kaboré et al., 2018), America (Crone et al., 2019; Kaboré et al., 2018; Kleywegt et al., 2020; Schwanz et al., 2016), Asia (Endirlik et al., 2019; Guardian et al., 2020; Heo et al., 2014; Kaboré et al., 2018; Kim et al., 2011; Kunacheva et al., 2010; Lam et al., 2017; Li et al., 2021; Qu et al., 2019), Europe (Atkinson et al., 2008; Boiteux et al., 2012; Harrad et al., 2019, 2020; le Coadou et al., 2017; Li et al., 2018; Llorca et al., 2012; Loos et al., 2007; Schwanz et al., 2016; Zafeiraki et al., 2015), and Oceania (Hepburn et al., 2019; Thompson et al., 2011) countries. Despite the widespread occurrence of PFAS, the regulation and monitoring of these contaminants is still in its early stages in many countries.

Currently, the scientific community is investigating the presence and scope of emerging contaminants in the environment and in drinking water. However, the public is not always aware of the risks associated with these emerging contaminants, which leads to inadequate action and involvement (Wee and Aris, 2019). Thus, this review provides a pioneering overview of the presence of PFASs in both environmental and drinking water contexts, delving deeply into the multifaceted toxicological ramifications of PFAS exposure. An extensive literature search was conducted using databases including Scopus and Google Scholar, encompassing references published from the 1980s to the present. The search strategy incorporated key terms such as 'PFAS exposure,' 'PFOA,' 'PFOS,' 'health effects,' 'toxicity,' 'surface water,' 'groundwater,' and 'drinking water' to identify pertinent studies within the field. Moreover, this review underscores the imperative necessity to devise robust and sustainable monitoring and management blueprints for PFAS, spanning their inception, application, release, and mitigation. Serving as a linchpin for galvanizing multi-stakeholder collaboration, this review addresses the escalating global challenge of PFAS contamination and fervently champions the formulation of holistic legislative and policy measures to rigorously evaluate and mitigate the risks associated with PFAS.

2. Sources and transport pathways

Global contamination by PFAS is a result of a wide range of industrial and consumer production, manufacturing, and applications (ITRC, 2020). This contamination arises from both primary manufacturing facilities, which produce and utilize PFAS to manufacture goods and generate environmental releases of PFAS through emission, dispersion, spills, and disposal of waste and wastewater. In addition to manufacturing facilities, the use of firefighting foams has also been linked to PFAS contamination in various environmental matrices, such as surface water, groundwater, drinking water, air, sediment, soil, and biota, under different practices and mechanisms (Bao et al., 2019; Chen et al., 2016a; Dong et al., 2020; Eschauzier et al., 2013; Filipovic et al.,

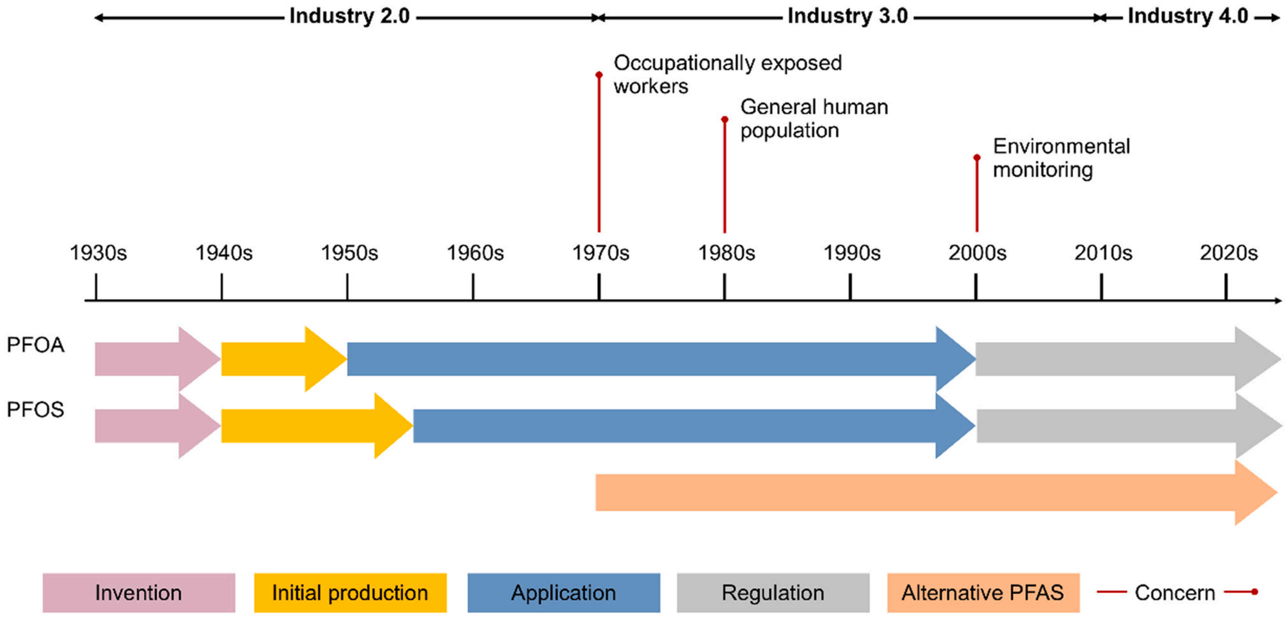

Fig. 1. Chronology of PFAS in terms of invention, production, application, concern (health and monitoring), and regulation. Following the discovery and early use of PFAS in the 1940s, there was a rapid increase in their production, diverse applications across industries, growing concerns about their adverse health effects and environmental persistence, with the establishment of regulatory frameworks targeted at managing and mitigating PFAS contamination.