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Review

Calling for a comprehensive risk assessment of selenium in drinking water

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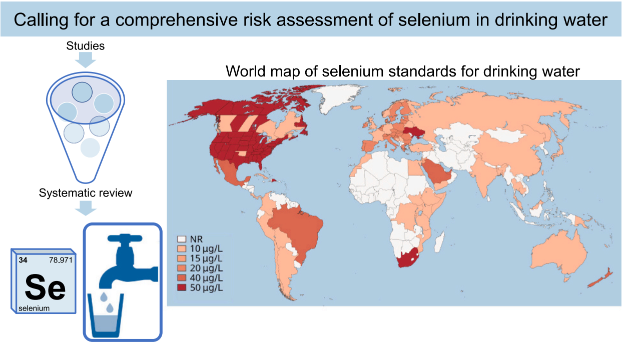
HIGHLIGHTS

- Drinking water selenium standards worldwide are scarce and conflicting.
- Most recent human and laboratory evidences indicate the need to re-assess selenium standard.
- Drinking water limit of around 5 μg/L of selenium is needed to protect human health.

GRAPHICAL ABSTRACT



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ABSTRACT

In the last two decades, research has elucidated that selenium, a trace element, has both nutritional and toxicological effects on human health, depending on its dose and chemical form. Recent animal, laboratory, and human studies have shown harmful effects of certain selenium species at specific exposure levels, prompting the need to reassess overall exposure to this element, including that occurring through drinking water, a primary source of inorganic selenium. Drinking water selenium standards worldwide are scarce and existing standards are inconsistent, likely because they have been informed by an incomplete and outdated assessment of the scientific evidence. Incorporating all the available human and laboratory evidence into a precautionary regulatory framework indicates that a drinking water limit of around 5 μg/L of selenium is needed to protect human health, i.e. with an uncertainty factor of 2 versus the lowest adverse effect level observed in human studies, and that higher values may pose unacceptable risks to humans. Despite the rarity of such high levels of selenium in underground and potable waters, coal mining and other sources of environmental pollution as well as geological factors may raise drinking water selenium content above a safe threshold, triggering the need to protect consumers, and to face challenging technological issues for selenium removal, currently under active investigation.

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1. Introduction

Water pollution is a major environmental and public health issue given the adverse effects of climate change and global warming on water quantity and quality (Filippini et al., 2024; Joseph et al., 2022). Trace elements, which are found in drinking water in addition to other sources of exposure, may adversely or beneficially affect human health, depending on amount of exposure, chemical form, duration of consumption, and interacting factors. Selenium is probably one of the most well-known of these elements (Vinceti et al., 2013a) alongside others such as fluoride and manganese (EFSA Panel on Nutrition Novel Foods Food Allergens et al., 2023b; Iamandii et al., 2024; Veneri et al., 2023). Selenium is a metalloid generally found in small amounts in underground waters, apart from major sources of environmental pollution or contaminated soil, such as those occurring in so-called seleniferous areas (Frisbie et al., 2015; Kumkrong et al., 2018; LeBlanc et al., 2018; Vinceti et al., 2013a; Vinceti et al., 2024). Selenium is also unique among the trace elements in having a narrow safe range of intake, and in being toxic to humans, animals, and the environment in doses slightly exceeding the nutritionally recommended ones (Naderi et al., 2021; Vinceti et al., 2017; Vinceti et al., 2018c), with recent evidence quickly accumulating about low-dose selenium toxicity in the human (Soares et al., 2024; Williams et al., 2025).

Given the dual effects of this element, efforts have been made by policy makers to identify the safe range of exposure based on human and animal studies. While there is a general consensus that the safe range is narrower than for any other essential element, the exact boundaries of this range and the selenium standard in drinking water in particular are still unclear and debated (Barron et al., 2009; Frisbie et al., 2015; Gilron, 2012; Kumkrong et al., 2018; Mitchell and Frisbie, 2023; Vinceti et al., 2013a; Vinceti et al., 2022b; Vinceti et al., 2018c). Herein, we summarize current knowledge about the human health effects of selenium in drinking water, providing a comprehensive overview of assessments of its standards in drinking water across countries, offering recommendations for future research in this area, and, based on the available evidence, endorsing a more adequate drinking water selenium limit to protect human health.

2. Selenium toxicity in humans: updated evidence with emphasis on drinking water

The last two decades have been characterized by important advancements in selenium research after experimental studies failed to show beneficial effects of the trace element on human health (Filippini et al., 2023a; Kelishadi et al., 2022; Vinceti et al., 2018a; Vinceti et al., 2018b). Concerns about selenium toxicity were generated by early studies investigating the nutritional benefits of selenium during 1990–2010, which prompted the implementation of several randomized controlled trials (RCT). The first of those trials, carried out in patients with non-melanoma skin cancer (Clark et al., 1996), failed to detect a beneficial effect of selenium supplementation on the primary outcome – i.e. incidence of non-melanoma skin cancer (Clark et al., 1996) and later demonstrated a detrimental effect on that outcome in a longer follow-up of the study population (Duffield-Lillico et al., 2003). Nonetheless, this RCT indicated a strong beneficial effect of selenium supplementation on incidence of secondary outcomes, i.e. prostate cancer and other site-specific cancers. Such results informed new recommendations to increase selenium exposure to reduce cancer and chronic disease risk (Combs and Gray, 1998; Ip, 1998; Rayman, 2002). However, subsequent high-quality RCTs carried out in the United States in the 2000s indicated that selenium does not protect against chronic disease risk, but rather increases the risk of high-grade prostate cancer, type 2 diabetes, and skin disease (Cardoso et al., 2019; Kristal et al., 2014; Lippman et al., 2009; Sakr et al., 2014; Shaheen et al., 2007; Vinceti et al., 2018a). These results among others prompted two recent updates, to the recommended upper levels of dietary selenium, one by the European Food Safety Authority in 2023 and the other by the Italian Society of Human Nutrition in 2024 (EFSA Panel on Nutrition Novel Foods Food Allergens et al., 2023a; SINU, 2024), although effort to modify dietary and drinking water recommendations are still in process. In addition, the last two decades have witnessed major advancements in selenium research, i.e., epidemiologic studies of selenium in drinking water (Vinceti et al., 2019; Vinceti et al., 2018d), and human and laboratory studies documenting the toxicity of different chemical forms of selenium (Filippini et al., 2018c; Filippini et al., 2023b; LeBlanc et al., 2018; Michalke et al., 2009; Rohn et al., 2018; Urbano et al., 2021; Vinceti et al., 2023b; Weekley and Harris, 2013).

2.1. Randomized controlled trials (RCTs)

RCTs have consistently shown that adding as little as 200 μg/day of selenium to a background daily intake on the order of 100 μg may increase incidence of type 2 diabetes by about 11 % (Vinceti et al., 2018b), an effect that wanes after supplementation is discontinued (Klein et al., 2011). Consistently, Mendelian randomization studies (Jia and Chen, 2024; Rath et al., 2021; Yarmolinsky et al., 2018; Zeng et al., 2024) have confirmed that genotypes associated with higher circulating selenium levels are associated with an excess risk of type 2 diabetes, ranging from +4 % to +27 %. Non-experimental studies, reviewed in 2021 (Vinceti et al., 2021b) but still accumulating (Li et al., 2024; Pang et al., 2024; Shao et al., 2022; Uddin et al., 2024; Weiss et al., 2024; Zhou et al., 2024), have also confirmed the positive association between selenium exposure and risk of diabetes and metabolic disturbances. However, these non-experimental studies have indicated that the risk of diabetes and other metabolic disturbances may already start to increase at around 80 μg of daily intake (Vinceti et al., 2021b), i.e. at lower amounts of exposure than those evaluated in the experimental studies, though still well above the recommended dietary intakes by the US Institute of Medicine of 55 μg/day (Institute of Medicine Food and Nutrition Board, 2000). RCTs have also shown that even low-dose overexposure to selenium induces adverse dermatological effects such as dermatitis and alopecia, and gastrointestinal disturbances such as nausea (Lippman et al., 2009; Vinceti et al., 2018a), as observed among individuals residing in seleniferous areas (Chawla et al., 2020; Fordyce, 2013; Fordyce, 1996; Vinceti et al., 2001).

2.2. A natural experiment about drinking water selenium

Natural experiments provide an opportunity to study the health effects of a substance that cannot be administered to humans because of ethical reasons or has not been tested in a long-term trial, thereby expediting research in this area (Lash et al., 2020). Natural experiments mirror experimental studies, particularly double-blinded RCTs, in the sense that nature simulates a randomized trial. By far the most well-known, paradigmatic example of a natural experiment is the study by John Snow in mid-XIX century in London, where he identified contaminated water as the source of a cholera outbreak in Soho by investigating the distribution of the disease-related deaths according to different sources of tap water in community residences (Fine et al., 2013; Lash et al., 2020).

A natural experiment in Northern Italy assessed the health effects of long-term exposure to selenium through drinking water (Vinceti et al., 2019; Vinceti et al., 2018d). In that setting, the long-term incidence of diseases associated with chronic consumption of drinking water with high selenium content have been compared with a similar population consuming tap water with low selenium content. This instance occurred in Reggio Emilia, Italy, where thousands of residents since 1972 had been inadvertently consuming municipal tap water provided by a local well with unusually high levels of selenium, around 8 μg/L, of geological origin and as expected in its inorganic hexavalent form, selenate (Vinceti et al., 1996; Vinceti et al., 1998; Vinceti et al., 1995). In comparison, tap water in the remaining part of the other municipality contained typical levels of selenium (<1 μg/L). The separation of tap water sources was due to the higher location of the southern part of the municipality, and the need to find a local, independent source of underground water to provide public tap water to local residents. The methodologic value of this scenario was that both populations – the population consuming high-selenium tap water and the remaining population of unexposed residents – were similar in terms of educational attainment, occupation, and race, and that tap water distributed in these two areas had the same chemical (and physical) composition, with the only difference being selenium content, thereby reducing potential for unmeasured confounding (Vinceti et al., 1995). In addition, the high selenium content in one of the two areas was unknown to residents and public health authorities until the 1980s.

Therefore, a long-term follow-up of the residents' exposure to this unusual source of selenium via drinking water was carried out, under the assumption that exposed residents might have benefitted from such exposure. The follow-up of the high-selenium cohort did not identify beneficial effects of this unintended selenium intervention on incidence or mortality from chronic disease (Vinceti et al., 1995; Vinceti et al., 1994), while showing excess incidence of lymphoid malignancies (particularly myeloma), melanoma, and two neurodegenerative diseases, amyotrophic lateral sclerosis and Parkinson's disease (Vinceti et al., 2016; Vinceti et al., 2019; Vinceti et al., 2000b; Vinceti et al., 2018d). Evidence supporting a positive association between selenium exposure and risk of these conditions has been provided (Adani et al., 2020; Kilness and Hochberg, 1977; Maass et al., 2018; Maass et al., 2020; Mandrioli et al., 2017; Vinceti et al., 2013c). Such effects were more pronounced among residents exposed for longer periods and higher amounts of high-selenium tap water, with a tendency for effects to wane over time after the interruption of the exposure.

So far, this is the only human study we are aware of that could assess the health effects of varying levels of selenium in drinking water, and what's more by comparing one population consuming tap water with low selenium levels to another one with unusually high selenium levels, close to one of the most common drinking water standards i.e. 10 μg/L. Therefore, this natural experiment allowed to study the health effects of moderately-elevated levels of selenium in the chemical form typically found in drinking water.

Though a few other studies have investigated various endpoints in relation to selenium in drinking water, mainly in the US (Tsongas and Ferguson, 1977; Tsongas and Ferguson, 1978; Valentine, 1997; Valentine et al., 1980; Valentine et al., 1978; Valentine et al., 1987a, 1987b), none comprehensively assessed the health effects of selenium exposure, given the few outcomes investigated and the lack of control for potential confounders (Vinceti et al., 2013a). In addition, even in seleniferous areas, high levels of selenium in drinking water were either not measured or not found in many cases, with exceptions (Barron et al., 2012; Dhillon and Dhillon, 2016; Fordyce, 1996; Fordyce et al., 2000b; Hira et al., 2004; Kumar and Riyazuddin, 2011; Vinceti et al., 2017; Vinceti et al., 2001).

2.3. *The relevance of chemical species*

There is large evidence from several human, animal, and environmental studies that the biological properties of selenium differ, even markedly, across chemical forms of the element (Acioly et al., 2024; Dauplais et al., 2024; Filippini et al., 2018c; Filippini et al., 2023b; Lazard et al., 2017; LeBlanc et al., 2018; Little et al., 2024; Mandrioli et al., 2017; Oo et al., 2022; Palace et al., 2024; Plateau et al., 2017; Uddin et al., 2024; Vinceti et al., 2022a; Vinceti et al., 2013b; Vinceti et al., 2018c; Vinceti et al., 2001; Weekley and Harris, 2013), and that diet, drinking water, air pollution, and smoking considerably influence exposure to the different selenium species (Filippini et al., 2018c; Vinceti et al., 2017). The chemical form may be even more relevant than other factors expected to markedly influence selenium activities, such as the amount of exposure and the presence of other factors interacting with selenium bioavailability and metabolism (Vinceti et al., 2018c). Since selenium in drinking water is typically inorganic and it occurs in the hexavalent form, a risk assessment of selenium in drinking water should be considered specific to this chemical species i.e. selenate. To our knowledge, there have been no efforts to regulate specific chemical forms of selenium (Vinceti et al., 2017). In part, this might be due to the limited evidence about the effects of inorganic selenium species in humans (Vinceti et al., 2018a). Conversely, for organic selenium, namely selenomethionine and the selenium form (mainly organic) present in selenized yeast, high-quality data are available from RCTs (Vinceti et al., 2018a). Large evidence is also available about how selenoprotein upregulation can be differentially induced by inorganic and organic selenium species, either for a higher bioavailability of the metalloid or by triggering a compensatory response to the pro-oxidant effects of selenium exposure itself (Jablonska and Vinceti, 2015; Vinceti et al., 2022b).

Toxicity depends on overall amount of exposure, the specific chemical form of the metalloid, on the endpoint and the animal/human species, and on concomitant exposures interacting with the selenium species. Such differences may be extremely relevant. For instance, acute neurotoxicity is 43-fold higher for inorganic tetravalent selenium compared with selenomethionine (Ammar and Couri, 1981), and a shift from 20 % to 80 % of animals (pigs) who became affected by paralytic signs and brain/spinal cord lesions moving from 25 μg/g of organic selenium to selenate has been documented in experimental conditions (Tsunoda et al., 2000). This indicates that caution should be used when comparing the upper level of selenium in foods (mostly in the organic form) with that of the inorganic form in drinking water. This also means that any risk assessment of dietary selenium, typically the main source of exposure, should not be generalized to drinking water. Although exposure to inorganic forms appears to be more harmful, confirmative data from RCTs are lacking, and will likely never become available given the ethical implications of administering selenium to humans (EFSA Panel on Nutrition Novel Foods Food Allergens et al., 2023a; Vinceti et al., 2018a; Vinceti et al., 2018c).

3. Human exposure to selenium through drinking water

The occurrence of different selenium species in drinking water has long been observed and investigated, though instances of severe selenium contamination of drinking water leading to short- and medium-term toxicity are rarely encountered (Vinceti et al., 2013a; Vinceti et al., 2023a; WHO, 2011b). Water used for human consumption typically includes only trace amounts of selenium, from an order of ng/L up to few μg/L, even in areas with elevated soil selenium content (Alfthan et al., 1992; Barron et al., 2012; Conde and Sanz Alaejos, 1997; Ćurković et al., 2016; Dhillon and Dhillon, 2003; Fordyce, 2005; Gourcy et al., 2010; Hu et al., 2009; Hudak, 2009; Hurtado-Jimenez and Gardea-Torresdey, 2007; Kuisi and Abdel-Fattah, 2010; Kumar and Riyazuddin, 2011; Wang et al., 1991; WHO, 2011b; Yanardag and Orak, 2001), though in some instances selenium water content may even exceed hundreds of μg/L (WHO, 2011b). Low selenium content also characterizes bottled waters (Ferri and Frasconi, 2006; Yanardag and Orak, 2001): for instance, nearly 97 % of samples in a large European study were below 5.5 μg/L, the detection limit of the analytical methodology (Bertoldi et al., 2011). Thus, there have been few public health 'emergencies' with reference to extremely high tap water selenium content, and in addition there is limited evidence and awareness about any adverse health effects induced by slightly elevated selenium content, on the order of a few μg/L, among consumers (Vinceti et al., 2023a; Vinceti et al., 2017). Though selenium exposure through drinking water is generally much lower than that from diet (EFSA NDA Panel, 2014; Filippini et al., 2018a; Vinceti et al., 2021a), the bioavailability and toxicity of selenium from these sources tend to be markedly different (Filippini et al., 2018c; Vinceti et al., 2012).

The main source of selenium in underground water and drinking water is generally the soil selenium content (Dhillon and Dhillon, 2016; Golubkina et al., 2018; Malhotra et al., 2022; Vinceti et al., 2023a; Vinceti et al., 2017; Zhao et al., 2017). Other factors may influence drinking water selenium levels, such as industrial pollution, mining (particularly coal mining), and agricultural drainage (Dos Santos et al., 2021; Hendry et al., 2024; Santos et al., 2019; Vinceti et al., 2013a; Vinceti et al., 2017). Removal of selenium, selenate in particular (Bueno et al., 2022; LeBlanc et al., 2018; Vinceti et al., 2010), from underground and drinking waters is difficult (Abejon, 2022; Ali and Shrivastava, 2021; Fadaei and Mohammadian-Hafshejani, 2023; He et al., 2018; Hendry et al., 2024; Ruj et al., 2022). Selenium may also occur in freshwaters at slightly elevated levels that may already have harmful implications on wildlife (Lemly, 1999; Lemly, 2014; Liu et al., 2022; Palace et al., 2024). In contrast, levels in sea and river waters are generally low (Yanardag and Orak, 2001).

4. Regulatory standards for selenium in drinking water

To provide an overview of the current evidence about safety of selenium exposure through drinking water, we sought to retrieve all human studies investigating the health effects of selenium through drinking water, and to assess the regulatory standards for drinking water worldwide. We addressed our first objective through a systematic literature search, citation chasing and the use of recent comprehensive reviews of the topic (EFSA Panel on Nutrition Novel Foods Food Allergens et al., 2023a; SINU, 2024; Vinceti et al., 2018c; Vinceti et al., 2021b). Our second objective was investigated through a Google search and citation chasing.

About the potential output of a systematic literature search about the health effects of selenium via drinking water, we registered in PROSPERO (CRD42024617172) its protocol, and we performed a PubMed search from inception through January 4, 2025. We structured the search strategy as follows: humans[MESH] AND (selenium[tiab] OR selenium[MESH] OR “Selenium Compounds”[MESH] OR “Organoselenium Compounds”[MESH]) AND (“drinking water” OR “groundwater”. We then exported the search results to the Rayyan web application for systematic reviews, screening the articles for relevance (Ouzzani et al., 2016). We initially retrieved 256 records, of which 23 were selected after title and abstract screening. Additionally, we manually performed citation chasing to retrieve 7 more relevant records. The detailed study selection process is described in the PRISMA flowchart depicted in Fig. 1. Out of the retrieved papers, there were 30 specifically investigating health-related endpoints following selenium exposure through drinking water (Andrews et al., 1980; Chawla et al., 2016; Filippini et al., 2020; Fordyce et al., 2000a; Fordyce et al., 2000b; Gauba et al., 1993; Johnson et al., 2013; Kikuchi et al., 1999; Lei et al., 2016; Nakaji et al., 2001; Shani et al., 1985; Tsongas and Ferguson, 1977; Tsongas and Ferguson, 1978; Valentine and Kang, 1988; Valentine et al., 1980; Valentine et al., 1987a; Vinceti et al., 2016; Vinceti et al., 2010; Vinceti et al., 2000a; Vinceti et al., 2019; Vinceti et al., 1996; Vinceti et al., 2000b; Vinceti et al., 1998; Vinceti et al., 1995; Vinceti et al., 1994; Vinceti et al., 2018d; Zha et al., 2022; Zhou et al., 2023; Zhou et al., 2024; Zierler et al., 1988). Surprisingly, all these studies or most of them were not considered in the assessments performed by regulatory and public health agencies worldwide including the World Health Organization (WHO) and Environmental Protection Agency (EPA) (Table 1), partially due to their publication after the definition of the selenium standards and partially due to the limitations in literature search and retrieval methods of these assessments.

We also sought to identify all existing drinking water selenium guidelines, recommendations and limits (overall, ‘standards’) issued by governing bodies in various geographic regions through a Google and PubMed search also including a gray literature search, and by citation chasing of papers/documents specifically addressing this issue (Kumkrong et al., 2018; Vinceti et al., 2018c). Overall, we were able to identify 51 standards issued by different countries/states, reported in Table 1 and Figs. 2 and 3, alongside the source of the figure defined as standard. Regarding US, Canada, and the European Union (EU), exceptions are also reported in Table 1, and include two states in the US, five provinces in Canada, two countries in the EU, and two UN agencies,

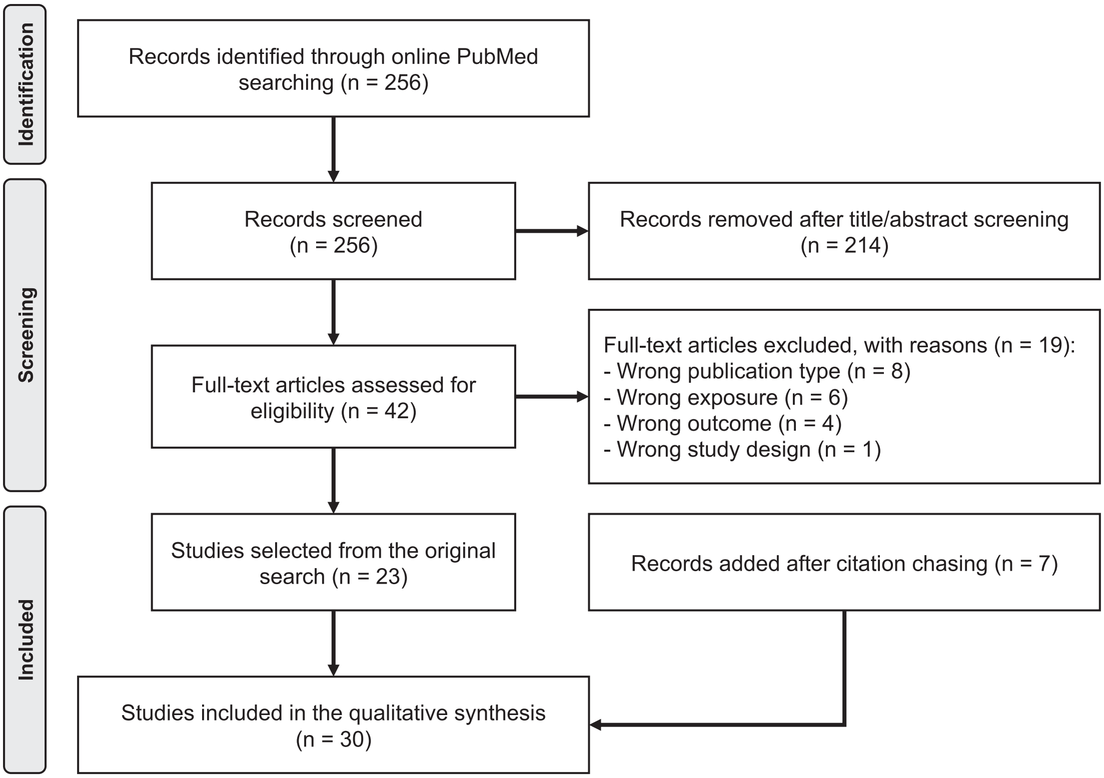

Fig. 1. PRISMA flow diagram illustrating the systematic search and selection of eligible studies on drinking water selenium.

Table 1
Limits and guidelines for the maximum amount of selenium in drinking water worldwide.

Country or Institution	Limit (μg/L)	Type of standard	Key details of human studies about selenium toxicity considered	Notes	Reference
Entities					
WHO (2011)	40	Provisional guideline	US - Smith & Westfall 1937, Rosenfeld & Beath 1964, Schrauzer & White 1978, Longnecker et al. 1991, Levander et al. 1997, Reid et al., 2004; Venezuela - Jaffe 1976; China - Yang et al., 1983 & 1989;	Max. 20 % of Upper Level (assuming 2 L/day of water consumption).	ISBN: 978–92–4-154,995-0 ISBN (2022, no assessment made): 978–92–4-004507-1
UNICEF (2008)	10	Guidance/reference document	NR		https://www.unicef.org/documents/2008-unicef-handbook-water-quality
Canada					
Health Canada (2014)	50	Guideline	Yang et al., 1983; Patterson and Levander, 1997; Yang et al., 1989a; Yang et al., 1989b; Yang and Zhou, 1994; Longnecker et al., 1991; Lemire et al., 2012; Jaffe et al., 1972; Hansen et al., 2004; Hurst et al., 2012; Rayman, 2012; Dennert et al., 2011; Duffield Lillico et al., 2003; Reid et al., 2008; L.C. Clark et al., 1996; L.C. Clark et al., 1998; Klein, 2003; Klein, 2009; Lippman et al., 2009; Bleys et al., 2008; Vinceti et al., 2000; Comstock et al., 1997; Willett et al., 1983; Allen et al., 2008; WHO and FAO, 2004; Fairweather-Tait et al., 2011; Boosalis, 2008; Flores-Mateo et al., 2006; Rayman et al., 2011; Stranges et al., 2006; Stranges et al., 2010; Rees et al., 2012; Bleys et al., 2008; Laclaustra et al., 2009; Laclaustra et al., 2010; Blankenberg et al., 2003; Freemantle, 2001; Brookes et al., 2004; Navarro-Alarcón et al., 1999; Stapleton, 2000; Kljai and Runje, 2001; Rajpathak et al., 2005; Bleys et al., 2007; Kornhauser et al., 2008; Akbaraly et al., 2010; Park et al., 2012; Czernichow et al., 2006; Bleys et al., 2007; Laclaustra et al., 2009; Stranges et al., 2007; Stranges et al., 2010; Rees et al., 2012; Vinceti et al., 2000; Hawkes and Turek, 2001; Hawkes et al., 2008; Hawkes et al., 2009; Vinceti et al., 2010; Bruhn et al., 2009; Thomson et al., 2005; Duffield et al., 1999.		ISBN: 978–1–100-23,001-6
Quebec (2024)	10	Legal limit	NR		https://www.legisquebec.gouv.qc.ca/en/document/cr/Q-2,%20r.%2040
Saskatchewan (2022)	10	Legal limit	NR		https://publications.saskatchewan.ca/api/v1/products/112863/formats/126899/download
New Brunswick (2018)	10	Legal limit	NR		https://community-prosperity-hub-fredericton.hub.arcgis.com/datasets/1bd199fada3d441b934abe967cde9360/explore
Ontario (2020)	10	Legal limit	NR		https://www.ontario.ca/laws/regulation/030169/v9?search=safe+drinking+water+act&use_exact=on
British Columbia (2018)	10	Legal limit	NR		https://www.bclaws.gov.bc.ca/civix/document/id/crbc/crbc/375_96_00_pit_2017_11_01
USA					
US EPA - large majority of states (2018)	50	Legal limit	NR		https://www.epa.gov/system/files/documents/2022-01/dwtable2018.pdf
California (2024)	50	Legal limit	NR	Up to 2010 Se limit was 10 μg/L (https://oehha.ca.gov/media/downloads/water/chemicals/phg/seleniumphg121010.pdf)	https://www.waterboards.ca.gov/drinking_water/certlic/drinkingwater/documents/lawbook/drinking-water-regulations-october-2024.pdf
Oklahoma (2020)	10	Legal limit	NR		https://www.epa.gov/sites/default/files/2014-12/documents/okwqs_chapter45.pdf

(*continued on next page*)

Table 1 (*continued*)

Country or Institution	Limit (μg/L)	Type of standard	Key details of human studies about selenium toxicity considered	Notes	Reference
Oceania					
Australia (2022)	10	Guideline	IARC (International Agency for Research on Cancer) (1987). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Overall Evaluations of Carcinogenicity. An updating of IARC monographs volumes 1 to 42. World Health Organization, IARC, Supplement 7; IPCS (International Programme on Chemical Safety) (1987). Selenium. Environmental Health Criteria, 58. World Health Organization, IPCS; Longnecker et al., 1991.		ISBN Online: 1864965118 (v3.8, 2022)
Papua New Guinea (2023)	10	Guideline	WHO Guidelines for drinking-water quality: fourth edition incorporating the first and second addenda.		https://www.washinhcf.org/wp-content/uploads/2024/07/WASH-GUIDELINE_2023.pdf
Fiji (2012)	10	Legal limit	NR		https://livelearn.org/assets/media/docs/resources/Fiji_MEHA_WinS_Standards.pdf
New Zealand (2022)	40	Legal limit	WHO Guidelines for drinking-water quality: fourth edition incorporating the first and second addenda.		https://www.legislation.govt.nz/regulation/public/2022/0168/latest/whole.html
Europe					
European Union (2020)	20	Legal limit		A parametric value of 30 μg/L shall be applied for regions where geological conditions could lead to high levels of selenium in groundwater.	https://eur-lex.europa.eu/eli/dir/2020/2184/oj
Switzerland (2014)	20	Legal limit	NR		https://www.vd.ch/fileadmin/user_upload/organisation/dse/scav/sire/Eaux_potables_Normes_Composition_chimique.pdf
Bosnia and Herzegovina (2010)	10	Legal limit	NR		https://faolex.fao.org/docs/pdf/bih148927.pdf
Serbia (2019)	10	Legal limit	NR		https://www.tehnologijahrane.com/pravilnik/pravilnik-o-higijenskoj-ispravnosti-vode-i
United Kingdom (2016)	10	Legal limit	NR		https://www.legislation.gov.uk/uksi/2016/614
Germany (2023)	10	Legal limit	NR		https://www.gesetze-im-internet.de/trinkwv_2023/
Iceland (2016)	10	Legal limit	NR		https://doi.org/10.1016/j.ijheh.2016.09.011
Norway (2016)	10	Legal limit	NR		https://lovdata.no/dokument/SF/forskrift/2016-12-22-1868
Russia (2002)	10	Legal limit	NR		https://www.mast.is/static/files/reglugerdir/sanpin_2_1_4_1175_02watersupply.pdf
Belarus (1999)	10	Legal limit	NR		https://schuchin-zhkh.by/assets/docs/%D0%A1%D0%B0%D0%BD%D0%9F%D0%B8%D0%9D%2010-124%20%D0%A0%D0%91%2099(2).docx
Ukraine (2013)	50	Legal limit	NR		https://waterlux.ua/promotions-and-news/trebovaniya-k-kachestvu-pitevoy-vody-sanpin-2-2-4-171-10/
Turkey (2014)	10	Legal limit	NR		https://www.fao.org/faolex/results/details/en/c/LEX-FAOC151040/
France (2020)	10	Legal limit	NR		https://draaf.occitanie.agriculture.gouv.fr/IMG/pdf/arrete_du_11_janvier_2007_cle0cea47-1.pdf
Central and South America					
Brazil (2021)	40	Legal limit	NR		https://bvsms.saude.gov.br/bvs/saudelegis/gm/2021/prt0888_07_05_2021.html
Chile (2005)	10	Legal limit	NR		https://www7.uc.cl/sw_educ/hidrologia/Capitulo_1/modulo1/nch409.html
Colombia (2013)	10	Legal limit	NR		https://alquimdecim.wordpress.com/wp-content/uploads/2013/10/normas_oficiales_para_la_calidad_del_agua_colombia.pdf
Costa Rica (2012)	10	Legal limit	NR		http://www.pgrweb.go.cr/scij/Busqueda/Normativa/Normas/nrm_texto_completo.aspx?param1=NRTC&nValor1=1&nValor2=72438&nValor3=90054&strTipM=TC

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Table 1 (*continued*)

Country or Institution	Limit (µg/L)	Type of standard	Key details of human studies about selenium toxicity considered	Notes	Reference
Cuba (2017)	10	Legal limit	NR		https://descargas.epconsgtmo.co.cu/Normalizacion%20Actualizadas/Normas%20de%20la%20construccion/Normas/OTRAS/nc_827_2017_agua_potable__requisitos_sanitarios__obligatoria_.nc_827_2017.pdf
Dominican Republic (2005)	50	Legal limit	NR		https://www.msp.gob.do/web/Transparencia/documentos_oai/163/decretos/3409/decreto-42-2005-que-establece-el-reglamento-para-aguas-de-consumo-humano.pdf
Ecuador (2011)	10	Legal limit	NR		https://spartaninter.com/wp-content/uploads/2023/07/INEN-1108-agua-potable.pdf
Panama (2007)	10	Legal limit	NR		https://silo.tips/download/ministerio-de-la-presidencia-decreto-n-136-de-martes-6-de-noviembre-de-2007
Peru (2011)	10	Legal limit	NR		http://www.digesa.minsa.gob.pe/publicaciones/descargas/Reglamento_Calidad_Agua.pdf
Mexico (2021)	40	Legal limit	NR		https://www.dof.gob.mx/nota_detalle.php?codigo=5650705&fecha=02/05/2022#gsc.tab=0
Bolivia (2004)	10	Legal limit	La Calidad del Agua Potable en América Latina - Ponderación de los Riesgos Microbiológicos contra los Riesgos de los Subproductos de la Desinfección Química. ILSI Argentina, OMS-OPS-1996		https://www.anesapa.org/data/files/NB512-AP_Requisitos.pdf
Argentina (2023)	10	Legal limit	NR		https://www.argentina.gob.ar/normativa/nacional/resoluci%C3%B3n-33-2023-394636/texto
Asia					
Abu Dhabi (2014)	40	Legal limit	NR		https://www.crystalline-uae.com/assets/pdf/municipalityguide/RSB-2014.pdf
Cambodia (2004)	10	Legal limit	NR		https://rdic.org/wp-content/uploads/2014/12/MIME-Drinking-Water-Quality-Standards-2004-en.pdf
China (2006)	10	Legal limit	NR		https://www.dgav.pt/wp-content/uploads/2022/06/China-GB-5749-2006_Standards-for-Drinking-Water-Quality.pdf
Taiwan (2022)	10	Legal limit	NR		https://oaout.moenv.gov.tw/law/EngLawContent.aspx?lan=E&id=295
Israel (2013)	10	Legal limit	NR		https://www.gov.il/BlobFolder/legalinfo/briut47/en/files_legislation_food_briut47-en.pdf
Japan (2003)	10	Legal limit	NR		https://www.nilim.go.jp/lab/bcg/siryou/tnn/tnn0264pdf/ks0264011.pdf
Jordan (2001)	15	Legal limit	NR		https://www3.dfc.gov/environment/eia/ammanwater/Annex%20C21-Drinking%20Water%20Standards.pdf
India (2012)	10	Legal limit	NR		https://cpcb.nic.in/wqm/BIS_Drinking_Water_Specification.pdf
Bangladesh (2019)	10	Legal limit	NR		https://dphe.gov.bd/site/page/15fa0d7b-11f1-45c0-a684-10a543376873/Water-Quality-Parameters-
Malaysia (2004)	10	Legal limit	WHO 1963		https://hq.moh.gov.my/engineering/images/perkhidmatan/kas/muat-turun/piawaian_kualiti_air_minum.pdf
Singapore (2019)	40	Legal limit	NR		https://sso.agc.gov.sg/SL/EPHA1987-S274-2019?DocDate=20190401&WholeDoc=1
Thailand (1978)	10	Legal limit	NR		https://wepa-db.net/archive/policies/law/thailand/std_drinking.htm
Yemen (2024)	10	Legal limit	NR		https://doi.org/10.1016/j.rechem.2024.101558
Saudi Arabia (2015)	40	Provisional guideline	NR		https://www.mwa.co.th/wp-content/uploads/2023/01/Water-Standard-2015.pdf
Africa					
South Africa (1996)	50	Guideline	APHA 1989. Standard Methods for the Examination of Water and Waste Water, 17th Edition. American Public Health Association, American Water Works Association, Water Pollution Control		https://www.iwa-network.org/filemanager-uploads/WQ_Compendium/Database/Selected_guidelines/041.pdf

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Table 1 (*continued*)

Country or Institution	Limit (μg/L)	Type of standard	Key details of human studies about selenium toxicity considered	Notes	Reference
			Federation. Published by the American Public Health Association, Washington DC, USA; BOWEN H.J.M. 1979. Environmental Chemistry of the Elements. Academic Press, London; McKEE J.E. and H.W. Wolf 1963. Water Quality Criteria, 2nd Edition. California State Water Resources Control Board, Publication No. 3-A. California; UNDERWOOD E.J. 1977. Trace Elements in Human and Animal Nutrition, 4th Edition. Academic Press, New York, USA; WEAST R.C. 1979. CRC Handbook of Chemistry and Physics, 60th Edition. CRC Press Inc., Boca Raton, Florida, USA; WORLD HEALTH ORGANIZATION 1984. Guidelines for Drinking Water Quality, Volume 2: Health Criteria and Other Supporting Information. World Health Organization, Geneva.		
Mozambique (2004)	10	Legal limit	NR		https://archive.gazettes.africa/archive/mz/2004/mz-government-gazette-series-i-dated-2004-09-15-no-37.pdf
Morocco (2018)	10	Legal limit	NR		https://www.onssa.gov.ma/wp-content/uploads/2022/10/CP03-DCPA-18-A_conditions-utilisation-des-eaux.pdf
Rwanda (2019)	10	Legal limit	NR		https://www.mininfra.gov.rw/fileadmin/user_upload/Mininfra/Documents/Water_and_Sanitation_docs/2_Rural_Drinking_Water_Quality_Framework.pdf
Egypt (2007)	10	Legal limit	NR		https://www.fao.org/faolex/results/details/en/c/LEX-FAOC083626/
Ethiopia (2013)	10	Legal limit	NR		https://www.cmpethiopia.org/content/download/1531/6997/file/Ethiopian%20Drinking%20Water%20Quality%20Standard%202013.pdf
East African Community (2022)	10	Recommendation	NR		https://www.tbs.go.tz/uploads/publications/en-1664261414-DEAS%2012%20-%202022%20Potable%20water.pdf
Uganda (2014)	10	Legal limit	NR		https://faolex.fao.org/docs/pdf/uga205721.pdf
Tanzania (2020)	10	Guideline	NR		https://www.ewura.go.tz/wp-content/uploads/2020/06/Water-and-Wastewater-Quality-Monitoring-Guidelines-2020.pdf

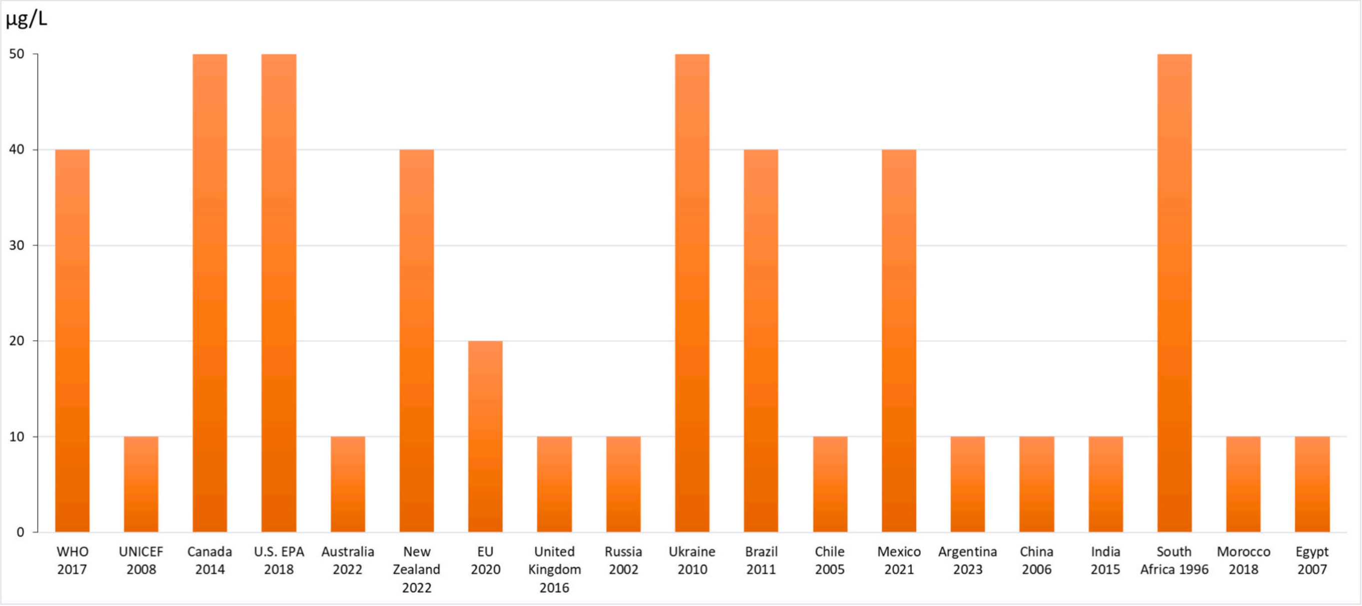

Fig. 2. Current drinking water selenium standards (limits, guidelines and recommendations as µg/L of all species of the element) across different agencies and countries.

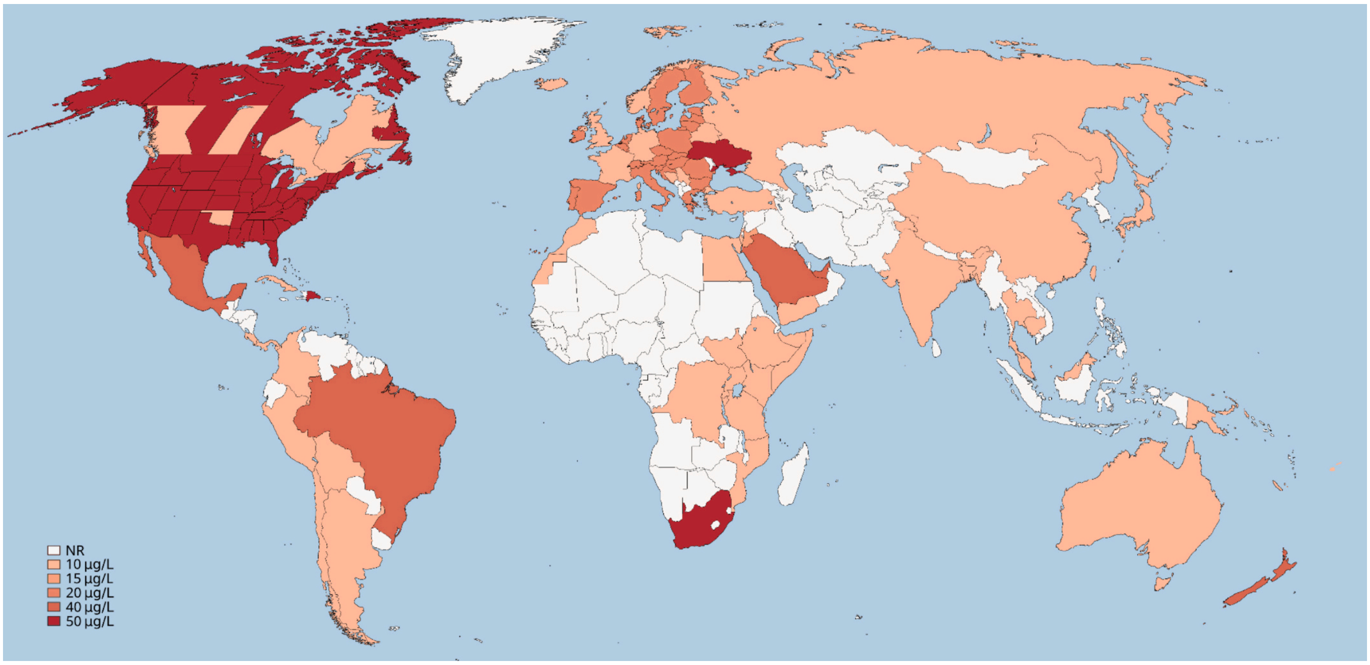

Fig. 3. World map of selenium standards (legal limits, guidelines and recommendations) for drinking water.

namely WHO and UNICEF. Those limits ranged from 10 to 50 µg/L, sometimes with marked differences even within the same country such as the US and Canada, with standards differing 5-fold, and what's more were issued a few years ago and could not take into consideration the most recent epidemiologic studies on the health effects of selenium. Unexpectedly, none of these regulations was allegedly based on a systematic search of the literature, nor did they evaluate the more recent body of evidence generated by peer-reviewed literature (Frisbie et al., 2015; Mitchell and Frisbie, 2023). Furthermore, 55 of the assessments did not report the source of evidence used to issue the limit, 5 (Australia, Bolivia, Malaysia, New Zealand, South Africa) reported other risk assessments as primary source of evidence, apparently sharing and incorporating their figures, and only 2 (WHO and Health Canada) carefully listed the human studies on selenium overexposure representing the body of evidence to base the assessment itself. However, these last two assessments did not mention how potentially relevant studies were taken into account and retrieved, selected, and integrated in the body of evidence that generated the selenium standards or recommendations, and both missed relevant papers. In addition, none of the available regulations mentioned performed a quality assessment of the human studies used to frame the standard, i.e. an evaluation of the risk of bias, the uncertainty and the imprecision of studies underpinning their assessment (Morgan et al., 2019; Murad et al., 2023; Schunemann et al., 2022). The WHO assessment defined its standard (actually, a guideline value) as a provisional one, possibly due to the lack of systematic literature search and appraisal of the evidence underlying it and the lack of (retrieved) epidemiologic studies on the specific effects of organic and inorganic selenium species (WHO, 2011, 2011b; Yan et al., 2020). This assessment also stated that the guideline figure of 40 μg/L was computed based on 20 % of the 2000 US-Institute of Medicine upper level of 400 μg/day and an estimated average of 2 L of water daily consumption in adults. However, no rationale for choice of cut point was provided, nor was the higher toxicity of inorganic selenium considered. According to such a statement, the recent reduction of the upper level for (dietary) selenium to 255 or 200 μg/day decided by the European Food Safety Authority (EFSA Panel on Nutrition Novel Foods Food Allergens et al., 2023a) and the Italian Society of Human Nutrition (SINU, 2024) would automatically decrease the drinking water guideline at least to 20 μg/L, assuming a rationale in such a 20 % figure. However, further reduction of such value seems recommended considering the new evidence discussed above.

5. Implications for risk characterization of drinking water selenium

Overall, we believe there is an urgent need for carefully conducted risk assessments that identify and summarize the relevant evidence from the literature to derive well-informed standards for safe levels of selenium exposure in drinking water.

Several factors likely contribute to the current gaps and limitations in the literature, including the rare occurrence of high levels of selenium in drinking water, the emphasis on understanding the nutritional value of selenium during the 1990s and 2000s, and the rarity of studies devoted to investigating the health effects of selenium in drinking water. However, long-term longitudinal studies on the health effects of inorganic selenium exposure through drinking water are now available, this being a potentially major methodological shift in the evidence base available for risk assessors. Such studies have shown that chronic exposure to tap water containing around 8–10 μg/selenium/day may increase incidence of specific neoplasms such as cancer of the buccal cavity and pharynx, lymphoid malignancies and melanoma, and of two neurodegenerative diseases, amyotrophic lateral sclerosis and Parkinson's disease (Vinceti et al., 2016; Vinceti et al., 2019; Vinceti et al., 2018d), linked to selenium overexposure on the basis of epidemiologic and toxicological evidence (Adani et al., 2020; Benatar et al., 2024; Filippini et al., 2018b; Maass et al., 2018). Given that the few other US studies investigating the health effects of selenium in drinking water (Tsongas and Ferguson, 1977; Valentine, 1997; Valentine et al., 1987b), as reviewed elsewhere (Vinceti et al., 2013a), were hampered by several limitations, among those related to exposure and outcome assessment, studies based on this natural experiment appear to be the only ones addressing the chronic effects of long-term consumption of inorganic selenium through drinking water.

Given the limitations of existing assessments, emerging evidence about the harmful effects of inorganic selenium exposure through drinking water at approximately 10 μg/L and of organic selenium from RCTs, we recommend a comprehensive reassessment of selenium exposure in drinking water. With this perspective we propose to apply the precautionary principle and divide by the above mentioned level by an uncertainty factor of 2. Thus, we propose setting a limit of 5 μg/L of selenium as a tentative new standard to protect against the harmful effects of long-term consumption of drinking water with inorganic selenium. Despite the relative rarity of water supplies with high selenium content, decreasing its levels is technologically challenging, since its removal requires the use of the best available technologies, currently under active investigation and apparently effective (Abejon, 2022; Lin et al., 2022; Malhotra et al., 2022; Shakya et al., 2024). Various treatment methods are currently available for the removal of selenium from water, including adsorption, bioremediation, photocatalysis, electrocoagulation, advanced oxidation processes, reverse osmosis, electrochemical techniques, ion exchange, centrifugation, chemical precipitation and coagulation (Ekwonna et al., 2024; Qu et al., 2023; Ruj et al., 2022). Among these, bioremediation by adsorption has recently gained considerable interest as a cost-effective alternative due to its potential for sustainable implementation, particularly through regeneration and reuse of the adsorbing media (Roy et al., 2024).

CRediT authorship contribution statement

Marco Vinceti: Resources, Project administration, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization, Writing – review & editing, Writing – original draft. **Riccardo Mazzoli:** Resources, Investigation, Formal analysis, Data curation, Writing – review & editing, Writing – original draft. **Lauren A. Wise:** Methodology, Writing – review & editing. **Federica Veneri:** Resources, Data curation, Writing – review & editing. **Tommaso Filippini:** Resources, Investigation, Formal analysis, Data curation, Conceptualization, Writing – review & editing.

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Declaration of competing interest

The authors declare no known competing financial interests or personal relationships likely to influence the work reported in this paper.

Data availability

The data that supports the findings of this study are available in this article.

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