Journal of Trace Elements in Medicine and Biology 98 (2026) 127965

Contents lists available at ScienceDirect

Journal of Trace Elements in Medicine and Biology

journal homepage: www.elsevier.com/locate/jtemb

Vanadium in environmental and biological systems: From industrial contaminant to insulin-mimetic agent

Jose L. Domingo

Universitat Rovira i Virgili, Laboratory of Toxicology and Environmental Health, School of Medicine, Sant Llorenç 21, Reus, Catalonia, 43201, Spain

ARTICLE INFO

Keywords:
Vanadium
Environmental contamination
Toxicology
Bioaccumulation
Phytoremediation
Insulin mimetic

ABSTRACT

Vanadium has emerged as a significant environmental contaminant of global concern, with increasing attention directed toward its complex biogeochemical behavior and potential health implications. This review provides a critical and integrative synthesis of environmental vanadium distribution, fate, and toxicological effects, with emphasis on speciation-dependent behavior, exposure pathways, and uncertainties in epidemiological inference. Vanadium exists in multiple oxidation states, with V(V) generally more mobile and often more toxic than V(IV), although toxicity is context-dependent. Industrial activities, particularly steel production, petroleum refining, and mining operations, contribute substantially to environmental vanadium loads. Environmental epidemiological studies have reported associations between vanadium exposure and adverse health outcomes, although exposure misclassification, co-pollutant confounding, and limited compound-specific data restrict causal inference. Recent cross-sectional evidence suggests associations between urinary vanadium and early kidney injury biomarkers in children, but longitudinal studies are needed to determine causality and clinical relevance. Paradoxically, in recent decades vanadium compounds showed promise as antidiabetic agents. However, serious concerns over long-term toxicity prevented their clinical application. Vanadium exhibits a dual role in biological systems, showing beneficial effects at low concentrations, while inducing oxidative stress and cytotoxicity at high levels. Phytoremediation and microbial bioremediation strategies are promising for environmental cleanup, with several plant species demonstrating hyperaccumulation capabilities. This review identifies critical knowledge gaps including limited understanding of vanadium speciation in marine environments, insufficient long-term epidemiological data, and the need for standardized risk assessment frameworks. Given the projected increase in vanadium applications, particularly in vanadium redox flow batteries (VRFBs) for energy storage, comprehensive environmental monitoring and regulatory frameworks are urgently required to mitigate potential risks to ecosystem and human health.

1. Introduction

Vanadium is rapidly becoming an important strategic resource due to changing industrial practices and emerging waste streams, marking its return to environmental prominence after a reduction in its historical primary source (fossil fuel emissions) since the 1970s [1,2].

The importance of vanadium in the functioning of land systems is extremely diverse, as this element may exert both positive and harmful effects on terrestrial organisms [3,4]. However, current knowledge remains fragmented, particularly regarding chronic low-dose exposure, chemical speciation, and long-term health outcomes. Vanadium has a variety of applications that make it suitable for use in ceramic production and decoration, production of pigments, an accelerator for drying paint, production of aniline black dye, and as a mordant in coloring textiles [5]. Taking advantage of its hardness, resilience, ability to form alloys, and its resistance to corrosion, vanadium is also used in the production of tools, steel, machinery, and surgical implants. In addition to its industrial applications, vanadium attracted considerable medical interest in the late 1980s and 1990s because of its insulin-mimetic properties. Moreover, some studies have also reported the medicinal utility of vanadium and its Schiff base complexes [6,7] reported that vanadium compounds have shown in vitro antiviral activity against several viruses, including influenza, HIV, and SARS-associated coronaviruses, although their clinical relevance remains uncertain. This author reviewed the potential beneficial effects of vanadium as a therapeutic agent for COVID-19, focused on its antiviral, anti-inflammatory, and antihyperglycemic effects. Of special relevance was the demonstration that vanadium had insulin-like properties in isolated cells and tissues,

E-mail address: joseluis.domingo@urv.cat.

https://doi.org/10.1016/j.jtemb.2026.127965
Received 1 May 2026; Received in revised form 13 August 2026; Accepted 24 September 2026
Available online 25 September 2026
0946-672X/© 2026 The Author(s). Published by Elsevier GmbH. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

Table 1
Selected vanadium concentrations in environmental matrices and human biological samples.

Matrix	Typical Range/Mean	Key Findings	References
Soil	10–220 mg kg^{-1}	Average concentrations typically 10–220 mg kg^{-1}; elevated in industrially contaminated areas	Hanus-Fajerska et al. [4]; Wang et al. [26]
Freshwater	0.076–0.285 mg L^{-1} (Panzhihua, China)	Heavily contaminated rivers near vanadium-mining and smelting zones	Zhang et al. [25]
Seawater	~1.5–2 μg L^{-1} (mean dissolved V)	2nd most abundant transition metal in seawater; ecological risk high especially in Asian waters; predominantly present as soluble V(V) vanadate oxyanions under oxic seawater conditions	Supe Tulcan et al. [24]
Marine sediments	—	Global review across 63 countries and 23 seas; ecological risk high especially in Asian seawater	Supe Tulcan et al. [24]
Urban air	Up to 10 ng m^{-3}	Rural ~1 ng m^{-3}; remote Pacific ~0.1 ng m^{-3}. In China, atmospheric emissions rose 86% over recent decades	Hanus-Fajerska et al. [4]; Zhang et al. [21]
Aquatic biota	—	Bioaccumulation documented in aquatic organisms; reviewed across global marine environments	Supe Tulcan et al. [24]
Human urine (occupational)	Up to 20.6 μg L^{-1}	vs. background ~2.7 μg L^{-1} in non-exposed controls; elevated NGAL in exposed children	ATSDR [27]; Rojas-Lima et al. [28]
Human blood/serum (general population)	~0.05 μg L^{-1} (background)	Normal reference concentration in non-exposed adults; substantially elevated in occupationally exposed workers (see urine row below for occupational biomonitoring data)	ATSDR [27]
Human cerebrospinal fluid (CSF)	Lower than plasma	CSF vanadium significantly lower than plasma/serum in Alzheimer's disease patients vs. healthy controls; blood (plasma/serum) remains the most frequently sampled matrix in neurodegenerative-disease research, CSF and brain less so	Gerhardsson et al. [29]; Ścibior et al. [30]

Values are not directly comparable across studies due to methodological heterogeneity. Concentration ranges are given where a single representative value could be attributed with confidence to a specific cited source. For marine sediments and aquatic biota, the cited global reviews report pooled, highly heterogeneous distributions across many countries and matrices rather than a single representative range, so a range is not given here to avoid oversimplification [24].

generating considerable interest in its potential therapeutic applications for diabetes mellitus [8–13]. However, concurrent with these findings, a critical body of evidence highlighted the substantial toxicological concerns associated with systemic vanadium exposure, particularly from chronic administration required for therapeutic purposes [14–16].

This narrative review offers an integrated and up-to-date overview of vanadium across environmental, biological, and medical contexts, with particular attention to recent findings that may alter current risk perspectives. In addition to summarizing established knowledge on environmental distribution, toxicological pathways, and past pharmacological applications, the review highlights novel epidemiological evidence indicating subclinical renal effects at background exposure levels, as well as advances in mechanistic research pointing to mitochondrial dysfunction. It also considers the growing relevance of vanadium in energy storage technologies, particularly vanadium redox flow batteries (VRFBs) [17]. By systematically linking chemical speciation, exposure routes, biological effects, and regulatory considerations within a coherent framework, this work extends existing literature and highlights key research gaps that warrant coordinated scientific and policy efforts in light of the expanding global use of vanadium.

2. Methods

A review based on scientific literature was conducted to identify relevant peer-reviewed publications using major academic databases, including PubMed, Scopus, Web of Science, and Google Scholar. It follows a structured narrative approach with an explicit search strategy and defined selection criteria. The search covered literature published through April 10, 2026. Key search terms included "vanadium," "environmental contamination," "speciation," "toxicology," "health effects," "diabetes," "insulin mimetic," "bioaccumulation," "phytoremediation," "vanadium redox flow batteries," "mitochondrial dysfunction," and "risk assessment." The reference list of retrieved articles was screened for additional relevant publications. Studies were selected based on their relevance to the scope of this review, with priority given to original research articles, high-quality reviews, and authoritative reports from governmental agencies. Inclusion criteria comprised peer-reviewed studies addressing environmental occurrence, toxicology, or epidemiology of vanadium. Studies lacking methodological transparency or relying solely on secondary citation were excluded.

3. Environmental sources and distribution

3.1. Natural and anthropogenic sources

Vanadium is released into the environment from both natural and anthropogenic sources. Natural sources include continental dust, marine aerosols, weathering of V-containing rocks, soil erosion, volcanic emissions, and wildfires, while anthropogenic sources include industrial wastes, combustion of fossil fuels, mining and processing of metal ores, technological applications, agricultural practices, and tanker disasters [18,19]. The use of vanadium in sulfuric acid production results in the release of soot and fly ash rich in vanadium pentoxide. Petroleum refining, smelting, welding, and cutting of vanadium-rich steel alloys, and the cleaning and repair of oil-fired boilers are additional sources of increased airborne V-bearing particles. Moreover, vehicular traffic and tobacco smoking are also pointed out as anthropogenic sources of environmental vanadium contamination [20]. A recent comprehensive emission inventory for China covering 2015–2019 quantified cumulative vanadium emissions of 211,095 tons into the atmosphere, 3725 tons into soil, and 0.1 tons into water from five major anthropogenic sectors. These figures represent cumulative totals over the 2015–2019 study period rather than annual estimates. The markedly lower water-borne emissions reflect a narrower source profile, wastewater treatment discharge being the principal contributor to the water pathway, compared with the broader combustion-related source base (coal combustion, stationary oil burning, and transportation) feeding atmospheric releases [21]. Coal combustion and stationary oil burning were identified as the largest contributors. These data confirm that atmospheric deposition is the dominant pathway by which anthropogenic vanadium enters terrestrial and aquatic systems [21].

3.2. Global distribution patterns

Global anthropogenic releases of vanadium to soil and water were re-evaluated by Hudson-Edwards et al. [1] and the rate at which this element was being deposited into the environment was increasing. Airborne concentrations of vanadium oxides in an urban environment can reach 10 ng m^{-3}, while in sparsely populated rural areas concentrations are about 1 ng m^{-3}, and above the eastern Pacific Ocean the mean vanadium air concentration is as low as 0.1 ng m^{-3} [4]. In China, cumulative atmospheric vanadium emissions have increased by 86%

over recent decades [21]. In the Panzhihua mining and smelting area of China, vanadium pollution of topsoil and sediments occurs mainly in the mining and extracting area, smelting area, slag dumping area, tailing dam, and coal mining area [22].

3.3. Environmental concentrations

Vanadium is a widespread trace element in the earth's crust, with average soil concentrations typically ranging from 10 to 220 mg kg^{-1} [4]. It is also widely distributed in marine environments, with concentrations varying significantly across different compartments due to both natural geological processes and anthropogenic activities like oil refining and power generation [23]. A comprehensive review of 260 studies across 63 countries and 23 seas revealed significant global vanadium contamination in marine ecosystems [24]. Surface water in the Panzhihua region, Southwestern China, contained vanadium concentrations ranging from 0.076 to 0.285 mg/L in the Jinsha River near a tailing impoundment, exceeding the recommended limit of 0.05 mg/L for drinking water sources [25]. A summary of selected vanadium concentrations across environmental matrices and biological samples is presented in Table 1.

4. Chemical speciation and environmental behavior

4.1. Oxidation states and chemical forms

The chemistry of vanadium is complex [31]. There are many forms of vanadium that can be found in the occupational and environmental setting. Vanadium exists in valence states ranging from −3 to + 5, and can be routinely encountered as various forms of vanadyl, vanadate, and oxides, including VO_2, VO_3, VO_4, as well as vanadium pentoxide (V_2O_5) [32]. In the environment, vanadium primarily exists in two oxidation states: tetravalent [V(IV)] and pentavalent [V(V)]. In terms of ionic charge, V(III) occurs mainly as the trivalent cation V^{3+} (comparatively rare under environmental conditions), V(IV) predominantly as the vanadyl cation VO^{2+}, and V(V) mainly as vanadate oxyanions (VO_2^+, $H_2VO_4^-$, HVO_4^{2-}, or VO_4^{3-}, depending on pH) [31,32]. Vanadium(V) is generally more mobile and often more toxic than V(IV), although toxicity depends on environmental conditions and chemical speciation [33]. The toxicologically significant compounds are vanadium pentoxide (V_2O_5), sodium metavanadate ($NaVO_3$), sodium orthovanadate (Na_3VO_4), vanadyl sulfate ($VOSO_4$), and ammonium vanadate (NH_4VO_3) [27].

4.2. Environmental transformation and mobility

Vanadium occurs as various chemical forms in the soil environment, and its biogeochemical behavior is influenced by soil conditions including redox potential, soil pH, organic matter content, and microbial activity [34,35]. The chemical speciation of vanadium in soil shows a dominance sequence of insoluble residue > organically bound > Fe (amorphous) oxide-bound > Mn oxide-bound > soluble component [36]. Soil pH, redox potential (ORP), organic matter content (OM), cation exchange capacity (CEC), and plant nutrient content can influence the oxidation state and forms of vanadium present, impacting bioavailability and toxicity [37]. In a recent review, Kumar et al. [38] have detailed the environmental fate of vanadium emphasizing that V(V) biogeochemical cycling in soil-plant systems remains poorly characterized, while critical information gaps persist regarding molecular mechanisms of V(V) detoxification and tolerance in organisms. This variability in speciation represents a major limitation for exposure assessment and risk characterization.

5. Environmental epidemiology and human health effects

5.1. Occupational exposure studies

Occupational studies have shown that urinary vanadium levels significantly increase in exposed workers. Male and female workers exposed to 0.1–0.19 mg/m^3 vanadium in a manufacturing setting had significantly higher urinary vanadium levels (20.6 μg/L) than non-occupationally exposed control subjects (2.7 μg/L) [27]. The American Conference of Governmental Industrial Hygienists (ACGIH) lists vanadium pentoxide with a TLV–TWA of 0.05 mg/m^3 for inhalable particulate matter, measured as vanadium, and classifies it as A3, a confirmed animal carcinogen with unknown relevance to humans [39].

5.2. Environmental exposure and health outcomes

Exposure of non-occupationally exposed individuals to vanadium is an increasing public health concern. Studies have reported associations between exposure to airborne V-bearing particles and increased risks, although causal inference remains limited [20]. Recent U.S. EPA systematic evidence mapping effort identified 95 epidemiological studies and 31 animal studies meeting PECO (Population, Exposure, Comparator, and Outcomes) criteria for inhalation exposure to vanadium and compounds [40]. Epidemiology studies mostly characterized exposure to total vanadium from unknown sources, while most animal studies evaluated inhalation exposure to vanadium pentoxide [41].

5.3. Respiratory effects

Vanadium pentoxide dust is the most common occupational exposure form. No studies have been found regarding fatalities in humans after inhalation exposure to vanadium. Nevertheless, increases in mortality have been reported in laboratory animals exposed to vanadium pentoxide [42]. Deaths occurred in rabbits exposed to 114 mg vanadium/m^3 for 1 h, but not at 43 mg vanadium/m^3. Exposure to 18 mg vanadium/m^3 resulted in death in three of five rats exposed for 6 days [27]. Intermediate-duration exposure resulted in deaths in rats at 9 mg vanadium/m^3 and mice at 18 mg vanadium/m^3. A decrease in survival was observed in mice chronically exposed to 2.2 mg vanadium/m^3 [27].

5.4. Neurological effects

Vanadium has been identified as a component of fine-particulate air pollution, with serious concerns for the central nervous system (CNS). Available data indicate that more attention should be paid to chronic diseases related to vanadium and to the assessment of environmental vanadium exposure. Although it cannot be excluded that vanadium may help identify subjects at higher risk of detrimental effects on the CNS, more extensive epidemiological studies are needed to conclusively link vanadium pollution with neurodegenerative processes in humans [30]. Recently, [43] reported a negligible influence of vanadium on glutamatergic transmission and GABAergic receptor activity, after a single administration to healthy mice. Blood (plasma/serum) has been the most frequently used biological matrix for determination of vanadium concentration in patients with neurodegenerative illnesses [30,44]. A smaller number of studies have also quantified vanadium in cerebrospinal fluid (CSF). In patients with Alzheimer's disease, CSF vanadium concentrations were significantly lower than in healthy controls, with no consistent alteration in plasma vanadium [29]. Concentrations reported in occupational cohorts in the present review specifically refer to urinary vanadium, whereas the blood/CSF studies cited here derive from separate, non-occupational clinical populations.

5.5. Cardiovascular effects

Associations between exposure to airborne vanadium-bearing particles and increased risks of hypertension, dysrhythmia, systemic inflammation, and hypercoagulation have been reported [20]. The potential for genotoxic and reprotoxic effects of vanadium compounds through occupational and environmental exposures has also been observed [45].

5.6. Carcinogenicity assessment

Deleterious health effects induced by inorganic vanadium compounds are linked with carcinogenic, immunotoxic, and neurotoxic effects [46]. In 2006, the IARC classified the evidence for the carcinogenicity of V_2O_5 as inadequate in humans and sufficient in experimental animals, placing the compound in Group 2B: possibly carcinogenic to humans [47]. This classification applies specifically to vanadium pentoxide and should not be generalized without qualification to all vanadium species or exposure scenarios. In 2008, the ACGIH included V_2O_5 in category A3: confirmed animal carcinogen with unknown relevance to humans. Available evidence concludes that vanadium is not clastogenic and only weakly mutagenic [48]. It has marked mitogenic activity affecting the distribution of chromosomes during mitosis and possibly causing aneuploidy [49]. However, evidence for a carcinogenic response of vanadium pentoxide in F344/N rats [50], or dose-related tumorigenic response in B6C3F1 mice [51] was not found.

A major limitation across epidemiological studies is the lack of compound-specific exposure data, as most investigations quantify total vanadium without distinguishing oxidation states or chemical forms.

6. Toxicological mechanisms

6.1. Oxidative stress and molecular targets

Vanadate is almost a structural and electronic analogue of phosphate, especially in the tetrahedral trianionic forms (VO_4^{3-} and PO_4^{3-}). In most living organisms, vanadate ions negatively influence the phosphate-metabolizing system by inhibiting phosphatases, phosphodiesterases, ribonucleases, ATPases, and other enzymes [4]. Reactive oxygen species (ROS) generated by Fenton-like reactions and during the intracellular reduction of V(V) to V(IV), primarily by NADPH, contribute to multiple vanadium-induced intracellular processes, including DNA cleavage, lipid peroxidation, and cell cycle arrest [52,53]. Oxidative damage and cell cycle delay induced by vanadium(III) in human peripheral blood cells has been reported at concentrations producing cytotoxic and genotoxic effects, characterized by decreased cell viability, increased DNA damage, and cell cycle arrest [54].

6.2. Mitochondrial dysfunction

A mechanistically important dimension of vanadium toxicology is its capacity to impair mitochondrial function. Vanadium exposure disrupts energy metabolism, enhances ROS generation within the mitochondrial respiratory chain, and triggers downstream oxidative stress that ultimately leads to genetic damage and alterations in cellular signaling [55,56]. These mitochondrial alterations contribute to vanadium's potential carcinogenic, immunotoxic, and neurotoxic properties, affecting the neurological, renal, immune, and reproductive systems. Since there are no specific antidotal treatments for vanadium intoxication, plant-derived metabolites with antioxidant, mitochondrial-targeted, and chelating properties have been investigated as potential protective agents [57]. Simple model organisms such as the nematode *Caenorhabditis elegans*, the fruit fly *Drosophila melanogaster*, and zebrafish *Danio rerio,* have shown to be versatile experimental platforms for studying vanadium-induced mitochondrial dysfunction, offering short generation times, conservation of essential biological pathways with mammals, and the availability of genetic tools [55]. In any case, integration of mitochondrial dysfunction with systemic toxicity remains insufficiently characterized.

6.3. Organ-specific toxicity

6.3.1. Renal effects

Vanadium is nephrotoxic in vivo [32,58]. Excessive vanadium exposure has been experimentally associated with toxicity affecting the kidneys, liver, skeleton, spleen, and nervous system, although the specific target organs and severity of effects depend strongly on the chemical form of vanadium, dose, route of exposure, and duration of exposure [27,59]. The nephrotoxicity of vanadium was ultimately the cause of the discontinuation of the BEOV (Bis(ethylmaltolato)oxovanadium(IV)) clinical program, due to renal changes resulting from the doses used in the preclinical safety program [16,60]. A landmark cross-sectional epidemiological study of 914 healthy children without any diagnosed disease demonstrated that subjects in the second and third tertiles of urinary vanadium concentration showed a significant increase in urinary NGAL (neutrophil gelatinase-associated lipocalin) levels, a sensitive early biomarker of renal tubular damage [28]. These findings provided, for the first time, evidence of vanadium-associated subclinical nephrotoxicity in a non-occupationally exposed pediatric population [28]. It was highlighted in an accompanying editorial as having direct implications for the assessment of vanadium risks in the context of expanding VRFB (Vanadium Redox Flow Batteries) technology [61].

6.3.2. Genotoxic and reproductive effects

The toxic profile of vanadium compounds is extensive, including hematological and biochemical alterations, nephrotoxicity, immunotoxicity, and reproductive and developmental toxicity [62,63]. Vanadium has shown genotoxic and mutagenic potential, including induction of chromosomal aberrations and aneuploidy-related endpoints in vivo, raising concern about long-term carcinogenic risk [45]. Tissue accumulation of vanadium in bone, kidney, spleen, and testes following prolonged oral administration represents a primary concern for any therapeutic application requiring lifelong treatment [15].

7. Vanadium compounds in diabetes treatment

This section is included because the pharmacological literature highlights the same toxicokinetic challenge that complicates environmental risk assessment: vanadium can influence key phosphate-dependent signaling pathways involved in cell regulation, yet prolonged systemic exposure raises concerns about tissue accumulation and potential organ toxicity.

7.1. Historical background and discovery

The therapeutic potential of vanadium in diabetes treatment has a long history dating back to 1899, when Lyonnet [64] reported the first data on the potential use of vanadium salts for the treatment of diabetes, suggesting some lowering of glucose levels without adverse effects. That study has been considered a "Phase 0" clinical trial [65,66]. In the last century, Shechter and Karlish [67] published the results of a study demonstrating the insulin-like activity of vanadate in rat adipocytes, initiating a new era of antidiabetic research with vanadium-containing compounds. However, the study by Heyliger et al. [11] sparked the interest of the scientific community in the potential beneficial effects of vanadium salts in the treatment of diabetes mellitus. The authors administered sodium orthovanadate in the drinking water of streptozotocin-induced diabetic rats, noting a reduction in the blood glucose concentrations, while it also prevented diabetes-associated depressed cardiac performance.

7.2. Mechanisms of insulin-mimetic action

7.2.1. Protein tyrosine phosphatase 1B (PTP1B) inhibition

Among the known protein tyrosine phosphatases (PTPs), protein tyrosine phosphatase 1B (PTP1B) has received considerable attention due to its role as a negative regulator of insulin signaling [68]. The enzyme negatively regulates the insulin action cascade by dephosphorylating the insulin receptor (IR) and insulin receptor substrate (IRS) [69]. PTP1B is upregulated in patients with Type 2 diabetes, and reducing its activity results in enhanced insulin receptor signaling and improved insulin sensitivity and glucose tolerance [70].

7.3. Development of organovanadium complexes

Initially, inorganic vanadium compounds such as vanadyl sulfate and sodium metavanadate were used in clinical trials, characterized by poor and variable gastrointestinal absorption, minor gastrointestinal distress as the main adverse effect, and inconsistent glycemic efficacy across small clinical studies [71,72]. Bis(maltolato)oxovanadium(IV) (BMOV) and bis (ethylmaltolato)oxovanadium(IV) (BEOV) were subsequently introduced as second-generation organovanadium complexes, showing two to three times greater bioavailability than vanadyl sulfate [72]. These were designed to prevent premature degradation, allow sufficient absorption, and reduce gastrointestinal toxicity. On the other hand, Ghalichi et al. [73] reviewed the effects of vanadium on diabetic dyslipidemia in diabetic animals. It was found that most studies confirmed the beneficial effects of different vanadium compounds in at least one of the parameters of lipid profile (mainly triglycerides and total cholesterol).

7.4. Clinical trials

A Phase I clinical trial of BEOV confirmed the safety and tolerability of single escalating oral doses (10–90 mg) in 40 non-diabetic volunteers [72]. A Phase IIa trial in seven type 2 diabetic subjects showed reductions in fasting blood glucose and HbA1c [72]. However, in January 2009, Akesis Pharmaceuticals discontinued the AKP-020 program due to renal changes observed in the preclinical safety program [60]. In longer-term studies, 14 type 1 diabetic patients receiving oral vanadyl sulfate (50–100 mg three times daily) for 30 months showed decreased daily insulin requirements and fasting blood sugar [74]. More recently, a randomized, double-blind, placebo-controlled trial in 44 obese type 2 diabetic patients demonstrated that vanadium-enriched yeast supplementation (0.9 mg/day V) for 12 weeks decreased fasting blood glucose and HbA1c and increased insulin sensitivity [65]. These findings should be interpreted cautiously given limited sample sizes and lack of long-term safety data.

7.5. Critical assessment: toxicity as the primary barrier

Despite close to 125 years of research, it has not been possible to identify a lead vanadium compound with clinical applicability [65]. In contrast, a critical body of literature has consistently highlighted that the therapeutic use of vanadium "is not necessarily exempt from concern" due to tissue accumulation and potential toxicity from chronic administration [16]. The toxic profile includes hematological and biochemical alterations, nephrotoxicity, immunotoxicity, and reproductive and developmental toxicity [15]. Tissue accumulation in bone, kidney, spleen, and testes represents a particular risk for a condition requiring lifelong treatment [14,75]. It should be noted that this toxicological profile derives predominantly from animal studies. In the limited human clinical trials conducted to date, reported adverse effects have largely been mild gastrointestinal symptoms, while the renal changes that led to discontinuation of the BEOV (AKP-020) programme were identified in preclinical (animal) safety testing rather than in the human trial participants themselves [60,72]. The conclusion is that given the numerous unresolved questions regarding long-term safety, including tissue accumulation, potential carcinogenicity, and developmental toxicity. the use of vanadium compounds in diabetic patients must be approached with extreme caution. In relation to this, Domingo and Gómez [16] concluded that vanadium administration for the treatment of human diabetes was misplaced. Large-scale pharmaceutical development of vanadium compounds has remained limited, likely due to a narrow therapeutic index, significant tissue accumulation, safety concerns related to renal function, and complex pharmacokinetics [76]. The narrow therapeutic index and tissue accumulation remain the primary barriers to clinical translation.

8. Ecological effects and bioaccumulation

8.1. Effects on terrestrial plants

Low concentrations of vanadium may exert hormetic effects on plant growth, while V reduces plant biomass and induces toxic effects on plant morphology at higher levels ($\geq$2 mg/L) [26]. Oxidative stress induced by ROS produced under vanadium stress is considered the main reason for vanadium toxicity to terrestrial and aquatic organisms [26]. Low levels of vanadium elevate plant height, root length, and biomass production due to enhanced chlorophyll biosynthesis, seed germination, and nitrogen assimilation. Notwithstanding, high vanadium concentrations disrupt energy metabolism, inhibit key enzymes, and lead to growth retardation, root and shoot abnormalities, and even plant death [37]. The threshold level of toxicity is highly plant species-specific. Vanadium mainly accumulates in plant roots with very limited translocation to shoots [77]. A recent review has highlighted the need for integrated biogeochemical and physiological studies to deepen understanding of V(V) dynamics in soil-plant systems [38].

8.2. Bioaccumulation in wildlife

Birds of prey, as end members of the trophic chain, are well-known biological indicators of serious environmental hazards. Various animal species serve as biomonitors of environmental contamination by vanadium [18], which is among the most abundant redox-active transition metals in seawater [78]. Ecological risk analysis has indicated medium and high hazards to aquatic species, with potential impacts to 55% of aquatic species in Asia from chronic exposure [24].

8.3. Effects on soil microorganisms

Although vanadium contributes to biological nitrogen fixation as a co-factor in some nitrogenases, high vanadium alters microbial community structures [79]. Decreased microbial richness and diversity in soil and reduced soil basal respiration have been found to correlate with vanadium pollution [25]. Recent studies on soil-plant systems have emphasized that microbial consortia, including *Pseudomonas* sp., *Geobacter metallireducens*, and *Methanosarcina mazei*, drive vanadium transformations through redox reactions, with V(V) reduction to less mobile V(IV) under anaerobic conditions and oxidation to soluble V(V) during aerobic mineral weathering [80].

9. Remediation strategies for vanadium contamination

9.1. Physical and chemical methods

Remediation of vanadium-contaminated soils can be achieved by physical, chemical, and biological methods [81–83]. Physical remediation includes soil replacement, thermal desorption, and electrokinetic remediation. Chemical remediation includes soil washing, chemical immobilization, and chemical reduction [84]. Chemical reduction reduces the highly toxic and mobile V(V) to the less toxic and mobile V(IV) using reducing agents such as Fe(II) and S^{2-} [34]. Water treatment technologies for vanadium removal include adsorption, microbiological treatment, chemical precipitation, solvent extraction, electrokinetic remediation, photocatalysis, coagulation, and membrane filtration [34].

9.2. Phytoremediation

9.2.1. Hyperaccumulator plants

Aihemaiti et al. [85] reported that *Setaria viridis* accumulated greater than 1000 mg kg^{-1} V in its shoots and exhibited a translocation factor > 1. Recent studies have explored phytoaccumulation mechanisms across

Table 2
Summary of vanadium toxicological endpoints, key findings, and relevant regulatory limits.

Endpoint / Organ	Key Findings	Regulatory Status / Limits	References
Respiratory	Animal: deaths in rabbits at $\geq$ 114 mg V/m^3 (1 h) and rats at 18 mg V/m^3 (6 days); chronic mortality in mice at 2.2 mg V/m^3 . Human: no documented inhalation fatalities; upper/lower respiratory tract irritation reported in occupational cohorts (Section 5.3).	OEL: 0.05 mg V_2O_5/m^3 (ACGIH/ NIOSH). V_2O_5 classified IARC Group 2B; ACGIH A3.	ATSDR [27]; McGregor [47]
Renal	Animal: nephrotoxicity well-documented in vivo; renal changes identified in preclinical (animal) safety testing led to discontinuation of the BEOV clinical programme. Human: in 914 healthy children, urinary V was positively associated with elevated NGAL, indicating subclinical nephrotoxicity at background exposure levels.	No specific environmental renal standard. BEOV programme discontinued (2009).	Domingo and Gómez [16]; Rojas-Lima et al. [28]
Neurological	Animal/mechanistic: V crosses the blood–brain barrier; associated with mitochondrial dysfunction and ROS generation in experimental models. Human: neuroinflammation and neurodegeneration-related protein accumulation reported in association with vanadium exposure; altered blood/CSF vanadium documented in Alzheimer's disease patients (Section 5.4).	No specific CNS-based regulatory limit. Insufficient long-term epidemiological data.	Ścibior et al. [30]
Genotoxic / Carcinogenic	Animal/in vitro: induces DNA strand breaks, chromosomal aberrations, and aneuploidy; weakly mutagenic, not clastogenic; oxidative damage and cell cycle arrest documented. Human: evidence for carcinogenicity is classified by IARC as inadequate in humans; the Group 2B classification rests on sufficient evidence in experimental animals (Section 5.6).	IARC Group 2B (V_2O_5, 2006); ACGIH A3.	Alcántara-Mejía et al. [54]; Ghosh et al. [48]; Leonard and Gerber [49]
Cardiovascular	Human: associations with hypertension, dysrhythmia, systemic inflammation, and hypercoagulation reported in populations exposed to airborne V-bearing particles. Animal: dedicated animal cardiovascular data are limited; mechanistic pathways are not yet fully characterized.	No specific cardiovascular-based limit.	Fortoul et al. [20]
Immunotoxic	Animal/in vitro: dual effects reported, immunosuppression via inhibition of cytokine-inducible functions and stimulation via increased cytokine production and inflammation. Human: direct human immunotoxicity data are limited; effects are largely inferred from in vitro and animal studies [46].	No specific immunotoxicity-based regulatory limit.	Zwolak and Zaporowska [46]
Reproductive / Developmental	Animal: developmental and teratogenic toxicity documented in animal studies; tissue accumulation in bone, kidney, spleen, and testes. Human: dedicated human reproductive/developmental toxicity data are lacking; accumulation risk is inferred from animal data and from chronic therapeutic administration in diabetes trials (Section 7.5).	Major concern for therapeutic use (chronic lifelong administration for diabetes).	Domingo [15,62]; Domingo and Gómez [16]

Toxicological endpoints are influenced by chemical speciation, dose, and exposure duration. Within each endpoint, findings are labelled by species/evidence type (Animal, Human, or Animal/in vitro) to distinguish the strength and origin of the evidence base.

native plants in vanadium titanium magnetite tailings that have undergone 51 years of natural restoration, identifying divergent phytoaccumulation strategies and relevant taxa [86]. Soil pH, organic matter, iron and aluminum oxides, phosphorus, calcium, and other coexisting elements all affect V bioavailability, toxicity, and plant uptake [37].

9.2.2. Enhanced phytoremediation techniques

Recent studies have found that the addition of coffee grounds mitigates heavy metal stress on ryegrass and improves remediation efficiency [87]. On the other hand, machine learning approaches have been applied to predict and optimize V^{5+} remediation outcomes [87]. *Pongamia pinnata*, a nitrogen-fixing legume, has also shown promise for remediation of vanadium titanium magnetite tailings [88]. The integration of phytoremediation with soil amendments and microbial assistance is considered a promising approach for decontamination of vanadium-polluted soils [80,89].

9.3. Microbial bioremediation

Geobacter metallireducens, *Shewanella oneidensis*, and some strains of *Pseudomonas* have been identified as effective vanadium-reducing microorganisms [4,90]. By contrast, *Pongamia pinnata* is a nitrogen-fixing plant, not a microorganism, and its role in vanadium remediation is addressed above as a phytoremediation species (Section 9.2.2). Microbial fuel cells (MFCs) represent a low-cost bioelectrochemical technology developed for purification of vanadium-contaminated water [91]. Novel metabolic pathways for bioelectrochemical vanadate reduction by *Thiobacillus denitrificans* without exogenous electron donor supplementation have recently been described [92]. Despite promising laboratory-scale results, scalability and long-term field performance remain major challenges.

10. Risk assessment and regulatory considerations

10.1. Regulatory limits and standards

ACGIH, OSHA, ATSDR, and NIOSH have each established occupational exposure limits to vanadium metal and its compounds [20]. A proposed maximum permissible occupational exposure level is 0.05 mg V/m^3 in dusts or fumes of V_2O_5 per 8-hour shift. The recommended limit for drinking water is 0.05 mg/L according to Chinese standards, which is exceeded in several industrial areas [25]. In contrast to the occupational framework, regulatory guidance for the general population remains limited. The WHO Guidelines for Drinking-water Quality do not include a health-based guideline value for vanadium [93]. The EFA was unable to establish a Tolerable Upper Intake Level for vanadium owing to insufficient data on chronic low-dose effects in humans [94]. In the United States, the EPA IRIS programme derived an oral reference dose (RfD) of 0.009 mg/kg/day for vanadium pentoxide, based on decreased hair cystine levels in a chronic rat study, but this value has not been formally adopted as an enforceable drinking-water or food standard [27]. Table 2 summarizes the key toxicological findings and regulatory status by organ/endpoint.

10.2. Dose-response and speciation considerations

Differential absorption and toxicity have been observed across inorganic vanadium compounds and oxidation states. Sodium metavanadate (V^{5+}) has greater gastrointestinal absorption and increased toxicity relative to vanadyl sulfate (V^{4+}) in rats and mice [95]. Furthermore, vanadium compounds in solution can convert readily between oxidation states as a function of pH, concentration, and redox potential [41]. Ecological risk analysis has indicated medium and high

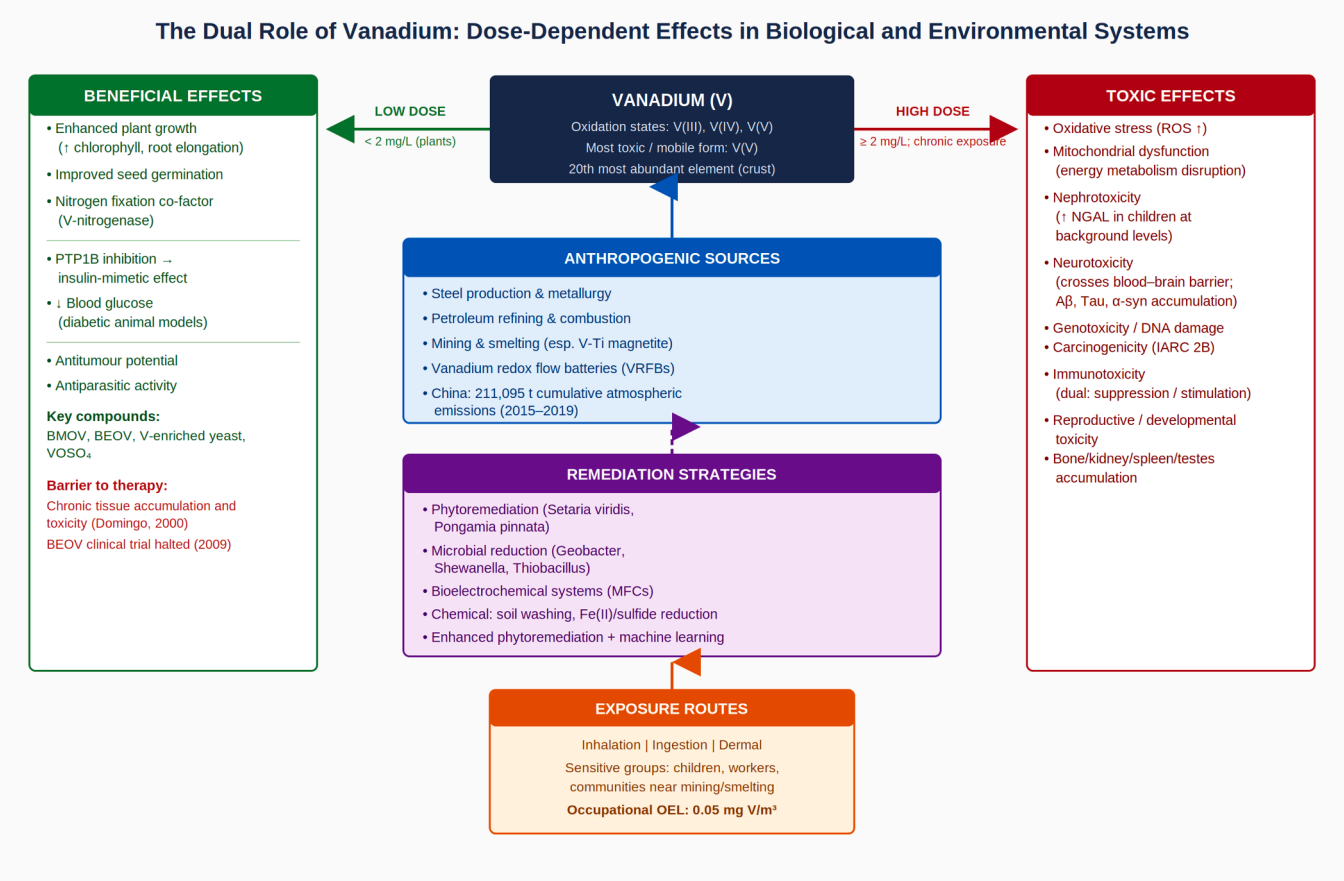


Fig. 1. The dual role of vanadium in biological systems: sources, dose-dependent effects, and health outcomes. Green cells indicate beneficial effects associated with low concentrations, while orange cells indicate adverse effects associated with elevated concentrations and chronic exposure. This figure should be interpreted within a speciation–exposure–mechanism framework.

hazards to aquatic species, principally from seawater [24]. Current regulatory frameworks do not adequately incorporate chemical speciation, representing a critical gap in risk assessment.

11. Emerging applications and future concerns

11.1. Vanadium redox flow batteries

Vanadium remains an important microalloying element in the metallurgical industry and has more recently become strategically important for energy storage. Vanadium redox flow batteries (VRFBs) are gaining traction as renewable energy deployment accelerates, and the vanadium market is projected to shift significantly with demand from the energy storage and steel sectors [96]. However, global supply remains constrained due to limited mining projects and geopolitical uncertainties, particularly relating to China and Russia as key producing nations. The environmental implications of expanded VRFB deployment (increased mining, processing, and potential environmental releases) warrant careful monitoring, particularly considering the early nephrotoxic effects in children even at background exposure levels [28,61]. Anyhow, lifecycle assessment of vanadium use in energy systems remains insufficiently developed.

11.2. Pharmaceutical applications beyond diabetes

Vanadium compounds have been proposed not only for the treatment of diabetes, but also for cancer and diseases caused by parasites [97–99]. Vanadium may exert inhibitory effects on cancer cell metastatic potential through modulation of cellular adhesive molecules and may reverse antineoplastic drug resistance [100]. These potential applications, while scientifically intriguing, require thorough toxicological characterization, particularly in light of the mitochondrial and renal toxicity profiles now better understood [28,55].

12. Conclusions and future perspectives

Vanadium represents a complex environmental contaminant with significant implications for both ecological and human health. Its dual nature (beneficial at low concentrations but toxic at elevated levels) highlights the critical importance of dose, chemical speciation, and exposure route in determining health outcomes [4]. The paradoxical role of vanadium as both a potential therapeutic agent for diabetes and an environmental toxicant further highlights this complexity. A key advance of this review is the integration of environmental chemistry, toxicology, and epidemiology within a unified framework.

Given the interconnected effects of vanadium across environmental compartments, food webs, wildlife, and human populations, a One Health framework offers a suitable foundation for future monitoring and risk management [3,4,26]. Adopting this approach could help integrate insights from environmental chemistry, ecotoxicology, exposure assessment, and public health to support the design of preventive measures and evidence-based regulatory policies [34,101].

The increasing industrial applications of vanadium, particularly in the context of VRFBs for renewable energy infrastructure, necessitate a proactive approach to environmental protection. Recent advances, including updated atmospheric vanadium emission inventories from China [21], evidence of early nephrotoxic effects in healthy children at background exposure levels [28], and mechanistic findings implicating

mitochondrial dysfunction as a key pathway of vanadium toxicity [55], collectively highlight the need for strengthened regulatory measures and sustained research efforts. Priority areas for future research include: a) development of standardized protocols for vanadium speciation analysis across different environmental matrices, b) comprehensive long-term cohort studies of chronic low-level exposure effects, particularly regarding neurodegenerative, renal, and developmental outcomes in vulnerable populations, c) further investigation of vanadium-induced mitochondrial dysfunction as a predictive biomarker, d) optimization of phytoremediation and microbial bioremediation for large-scale environmental cleanup, and e) development of a regulatory framework that accounts for chemical speciation, exposure pathways, and sensitive populations, especially children, who may experience subclinical kidney damage at environmental background concentrations.

The studies here reviewed show that vanadium pollution poses significant risks to environmental and human health, while simultaneously showing certain potential for possible beneficial applications. Future research should prioritize longitudinal studies, speciation-resolved exposure assessment, and mechanistic integration across biological systems. As industrial applications continue to expand, coordinated efforts among researchers, regulators, and industry stakeholders are essential to prevent widespread environmental contamination and protect public health.

Abbreviations

ACGIH: American Conference of Governmental Industrial Hygienists; ATSDR: Agency for Toxic Substances and Disease Registry; BEOV: Bis(ethylmaltolato)oxovanadium(IV); BMOV: Bis(maltolato)oxovanadium(IV); CEC: Cation Exchange Capacity; CNS: Central Nervous System; IARC: International Agency for Research on Cancer; IRS: Insulin Receptor Substrate; MFCs: Microbial Fuel Cells; NGAL: Neutrophil Gelatinase-Associated Lipocalin; NIOSH: National Institute for Occupational Safety and Health; NTP: National Toxicology Program; OM: Organic Matter; ORP: Oxidation-Reduction Potential; OSHA: Occupational Safety and Health Administration; PTP1B: Protein Tyrosine Phosphatase 1B; PTPs: Protein Tyrosine Phosphatases; ROS: Reactive Oxygen Species; T2D: Type 2 Diabetes; USEPA: United States Environmental Protection Agency; VRFBs: Vanadium Redox Flow Batteries.

Declaration of Generative AI and AI-assisted technologies in the writing process

Artificial Intelligence (Skywork AI Smart Slide Tool) was used to assist in the graphic design of Fig. 1.

Funding

This review was conducted without specific funding support and represents an independent synthesis of the available scientific literature on vanadium environmental and toxicological effects.

Declaration of Competing Interest

The author declares that he has no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. Jose L Domingo author of the current submission to JTEMB declares that he has no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Not applicable.

References

[1] K.A. Hudson-Edwards, P. Byrne, G. Bird, P.A. Brewer, I.T. Burke, H.E. Jamieson, M.G. Macklin, R.D. Williams, Origin and fate of vanadium in the Hazeltine Creek Catchment following the 2014 mount polley mine tailings spill in British Columbia, Canada, Environ. Sci. Technol. 53 (8) (2019) 4088–4098, https://doi.org/10.1021/acs.est.8b06391.

[2] T. Arora, N. Angnihotri, M. Azam, Vanadium's journey from essential trace metal to emerging environmental pollutant in the Anthropocene era, Turk. J. Chem. 50 (2026) 112–132, https://doi.org/10.55730/1300-0527.3785.

[3] L. Evans, A. Stokes, S. Griffin, Vanadium: environmental hazard or environmental opportunity? A perspective on some key research needs, Environmental Science Processes & Impacts 23 (4) (2021) 527–534, https://doi.org/10.1039/D0EM00470G.

[4] E. Hanus-Fajerska, A. Wiszniewska, I. Kamińska, A dual role of vanadium in environmental systems—beneficial and detrimental effects on terrestrial plants and humans, Plants 10 (6) (2021) 1110, https://doi.org/10.3390/plants10061110.

[5] M. Imtiaz, M.S. Rizwan, S. Xiong, H. Li, M. Ashraf, S.M. Shahzad, M. Shahzad, M. Rizwan, S. Tu, Vanadium, recent advancements and research prospects: a review, Environ. Int. 80 (2015) 79–88, https://doi.org/10.1016/j.envint.2015.03.018.

[6] K. Hashmi, S. Gupta, A. Siddique, T. Khan, S. Joshi, Medicinal applications of vanadium complexes with Schiff bases, J. Trace Elem. Med. Biol. 79 (2023) 127245, https://doi.org/10.1016/j.jtemb.2023.127245.

[7] S. Semiz, Vanadium as potential therapeutic agent for COVID-19: A focus on its antiviral, anti-inflammatory, and antihyperglycemic effects, J. Trace Elem. Med. Biol. 69 (2022) 126887, https://doi.org/10.1016/j.jtemb.2021.126887.

[8] S.M. Brichard, Effects of vanadate on the expression of genes involved in fuel homeostasis in animal models of Type I and Type II diabetes, Mol. Cell. Biochem. 153 (1) (1995) 121–124, https://doi.org/10.1007/BF01075926.

[9] A.B. Goldfine, M.E. Patti, L. Zuberi, B.J. Goldstein, R. LeBlanc, E.J. Landaker, Z. Y. Jiang, G.R. Willsky, C.R. Kahn, Metabolic effects of vanadyl sulfate in humans with non—insulin-dependent diabetes mellitus: in vivo and in vitro studies, Metabolism 49 (3) (2000) 400–410, https://doi.org/10.1016/S0026-0495(00)90418-9.

[10] I. Goldwaser, D. Gefel, E. Gershonov, M. Fridkin, Y. Shechter, Insulin-like effects of vanadium: basic and clinical implications, J. Inorg. Biochem. 80 (1–2) (2000) 21–25, https://doi.org/10.1016/S0162-0134(00)00035-0.

[11] C.E. Heyliger, A.G. Tahiliani, J.H. McNeill, Effect of vanadate on elevated blood glucose and depressed cardiac performance of diabetic rats, Science 227 (4693) (1985) 1474–1477, https://doi.org/10.1126/science.3156405.

[12] S. Ramanadham, J.J. Mongold, R.W. Brownsey, G.H. Cros, J.H. McNeill, Oral vanadyl sulfate in treatment of diabetes mellitus in rats, Am. J. Physiol. 257 (3) (1989) H904–H911, https://doi.org/10.1152/ajpheart.1989.257.3.H904.

[13] A.K. Srivastava, M.Z. Mehdi, Insulino-mimetic and anti-diabetic effects of vanadium compounds, Diabet. Med. 22 (1) (2005) 2–13, https://doi.org/10.1111/j.1464-5491.2004.01381.x.

[14] J.L. Domingo, Vanadium and diabetes. What about vanadium toxicity? Mol. Cell. Biochem. 203 (1–2) (2000) 185–187, https://doi.org/10.1023/a:1007067011338.

[15] J.L. Domingo, Vanadium and tungsten derivatives as antidiabetic agents: a review of their toxic effects, Biol. Trace Elem. Res. 88 (2) (2002) 97–112, https://doi.org/10.1385/BTER:88:2:097.

[16] J.L. Domingo, M. Gómez, Vanadium compounds for the treatment of human diabetes mellitus: a scientific curiosity? A review of thirty years of research, Food Chem. Toxicol. 95 (2016) 137–141, https://doi.org/10.1016/j.fct.2016.06.030.

[17] A.L. Akman, M.Z. Arslan, M. Farsak, The rise of vanadium redox flow batteries: a game-changer in energy storage, J. Alloy. Compd. 1038 (2025) 182869, https://doi.org/10.1016/j.jallcom.2025.182869.

[18] A. Ścibior, E. Wnuk, D. Gołębiowska, Wild animals in studies on vanadium bioaccumulation—potential animal models of environmental vanadium contamination: a comprehensive overview with a Polish accent, Sci. Total. Environ. 785 (2021) 147205, https://doi.org/10.1016/j.scitotenv.2021.147205.

[19] E. Wnuk, Mobility, bioavailability, and toxicity of vanadium regulated by physicochemical and biological properties of the soil, J. Soil. Sci. Plant Nutr. 23 (1) (2023) 1130–1149, https://doi.org/10.1007/s42729-023-01130-9.

[20] T.I. Fortoul, M. Rojas-Lemus, V. Rodriguez-Lara, A. Gonzalez-Villalva, M. Ustarroz-Cano, G. Cano-Gutierrez, S.E. Gonzalez-Rendon, L.F. Montaño, M. Altamirano-Lozano, Overview of environmental and occupational vanadium exposure and associated health outcomes: an article based on a presentation at the 8th International Symposium on Vanadium Chemistry, Biological Chemistry, and Toxicology, Washington DC, August 15–18, 2012, J. Immunotoxicol. 11 (1) (2014) 13–18, https://doi.org/10.3109/1547691X.2013.789940.

[21] H. Zhang, B. Zhang, B. Jiang, Q. Li, X. Hu, Y. Xing, Emission inventory development for spatiotemporal release of vanadium from anthropogenic sources in China, Atmos. Chem. Phys. 25 (2025) 5577–5589, https://doi.org/10.5194/acp-25-5577-2025.

[22] Y. Teng, J. Yang, Z. Sun, J. Wang, R. Zuo, J. Zheng, Environmental vanadium distribution, mobility and bioaccumulation in different land-use Districts in Panzhihua Region, SW China, Environ. Monit. Assess. 176 (1) (2011) 605–620, https://doi.org/10.1007/s10661-010-1607-0.

[23] K. Pyrzynska, T. Wierzbicki, Determination of vanadium species in environmental samples, Talanta 64 (4) (2004) 823–829, https://doi.org/10.1016/j.talanta.2004.05.007.

[24] R.X. Supe Tulcan, W. Ouyang, C. Lin, M. He, B. Wang, X. Xu, Vanadium pollution and health risks in marine ecosystems: anthropogenic sources over natural contributions, Water Res. 207 (2021) 117838, https://doi.org/10.1016/j.watres.2021.117838.
[25] B. Zhang, H. Zhang, W. Yan, H. Liu, Y. Chen, Z. Li, S. Zhou, Microbial community responses to vanadium distributions in mining geological environments and bioremediation assessment, J. Geophys. Res. Biogeosciences 124 (3) (2019) 601–615, https://doi.org/10.1029/2018JG004670.
[26] M. Wang, B. Zhang, H. Zhang, R. Geng, Y. Huang, J.Y. Yang, Y. Teng, Ecological and health risks of vanadium in the biogeosphere, Rev. Environ. Contam. Toxicol. 262 (1) (2024) 13, https://doi.org/10.1007/s44169-024-00065-1.
[27] ATSDR, Agency for Toxic Substances and Disease Registry. Toxicological Profile for Vanadium. U.S. Department of Health and Human Services. Atlanta, GA, 2012. https://www.ncbi.nlm.nih.gov/books/NBK592340/ (Available at).
[28] E. Rojas-Lima, M. Ortega-Romero, O.G. Aztatzi-Aguilar, J.C. Rubio-Gutiérrez, J. Narváez-Morales, M. Esparza-García, P. Méndez-Hernández, M. Medeiros, O. C. Barbier, Vanadium exposure and kidney markers in a pediatric population: a cross-sectional study, Pediatr. Nephrol. 40 (5) (2024) 1689–1700, https://doi.org/10.1007/s00467-024-06561-9.
[29] L. Gerhardsson, T. Lundh, L. Minthon, E. Londos, Metal concentrations in plasma and cerebrospinal fluid in patients with Alzheimer's disease, Dement. Geriatr. Cogn. Disord. 25 (6) (2008) 508–515, https://doi.org/10.1159/000129365.
[30] A. Ścibior, J. Llopis, P.P. Dobrakowski, T. Męcik-Kronenberg, CNS-related effects caused by vanadium at realistic exposure levels in humans: a comprehensive overview supplemented with selected animal studies, Int. J. Mol. Sci. 24 (10) (2023) 9004, https://doi.org/10.3390/ijms24109004.
[31] D.C. Crans, J.J. Smee, E. Gaidamauskas, L. Yang, The chemistry and biochemistry of vanadium and the biological activities exerted by vanadium compounds, Chem. Rev. 104 (2) (2004) 849–902, https://doi.org/10.1021/cr020607t.
[32] D.G. Barceloux, Vanadium, Journal Toxicology Clinical Toxicology 37 (2) (1999) 265–278, https://doi.org/10.1081/clt-100102425.
[33] N. Panichev, K. Mandiwana, D. Moema, R. Molatlhegi, P. Ngobeni, Distribution of vanadium(V) species between soil and plants in the vicinity of vanadium mine, J. Hazard. Mater. 137 (2) (2006) 649–653, https://doi.org/10.1016/j.jhazmat.2006.02.028.
[34] L. Chen, J.R. Liu, W.F. Hu, J. Gao, J.Y. Yang, Vanadium in soil-plant system: Source, fate, toxicity, and bioremediation, J. Hazard. Mater. 405 (2021) 124200, https://doi.org/10.1016/j.jhazmat.2020.124200.
[35] J.P. Gustafsson, Vanadium geochemistry in the biogeosphere—speciation, solid-solution interactions, and ecotoxicity, Appl. Geochem. 102 (2019) 1–25, https://doi.org/10.1016/j.apgeochem.2018.12.027.
[36] C. Li, Q. Zhang, Y. Luo, P. Christie, Environmental geochemistry and ecological risk of vanadium pollution in Panzhihua mining and smelting area, Sichuan, China, Chin. J. Geochem. 25 (4) (2006) 379–385, https://doi.org/10.1007/s11631-006-0378-3.
[37] A. Aihemaiti, Y. Gao, Y. Meng, X. Chen, J. Liu, H. Xiang, Y. Xu, J. Jiang, Review of plant-vanadium physiological interactions, bioaccumulation, and bioremediation of vanadium-contaminated sites, Sci. Total Environ. 712 (2020) 135637, https://doi.org/10.1016/j.scitotenv.2019.135637.
[38] A. Kumar, V. Kumar, H. Kaur, M. Thakur, A. Sharma, M. Radziemska, R. Kumar, Vanadium in the environment: biogeochemical cycling, bioavailability, speciation and detoxification mechanisms, Pedosphere (Press.) (2026), https://doi.org/10.1016/j.pedsph.2026.01.006.
[39] ACGIH, American Conference of Governmental Industrial Hygienists. (2008). Vanadium pentoxide. Available at: https://www.acgih.org/vanadium-pentoxide/ (accessed April 2, 2026).
[40] US EPA, A systematic review approach to assess the human health evidence for inhalation exposure to vanadium and compounds (EPA/635/R-24/001). Washington. DC: U.S. Environmental Protection Agency, 2024. https://assessments.epa.gov/risk/document/&deid=360944 (Available at_).
[41] S. Vulimiri, K. Newhouse, E. Yost, F. Branch, E. Radke-Farabaugh, J. Lee, A Systematic Review Approach to Assess the Human Health Hazards of Inhalation Exposure to Vanadium and Compounds (September). Environmental Mutagenesis & Genomics Society 54th Annual Meeting, Chicago, IL, Chicago, IL, 2023, https://assessments.epa.gov/risk/document/&deid%3D360944 (September).
[42] M. Rojas-Lemus, N. López-Valdez, P. Bizarro-Nevares, A. González-Villalva, M. Ustarroz-Cano, A. Zepeda-Rodríguez, F. Pasos-Nájera, I. García-Peláez, N. Rivera-Fernández, T.I. Fortoul, Toxic effects of inhaled vanadium attached to particulate matter: a literature review, Int. J. Environ. Res. Public. Health 18 (16) (2021) 8457, https://doi.org/10.3390/ijerph18168457.
[43] M. Sowa-Kućma, P. Pańczyszyn-Trzewik, N. Gałka, B. Bobula, K. Stachowicz, Vanadium shows no effect in stress-induced hyperthermia and the tail suspension test in healthy mice, J. Trace Elem. Med. Biol. (2025) 127742, https://doi.org/10.1016/j.jtemb.2025.127742.
[44] V.P. Sampath, S.V. Singh, I. Pelov, N. Horesh, H. Zannadeh, O. Tirosh, Y. Erel, D. Lichtstein, Vanadium in Bipolar Disorders—Reviving an Old Hypothesis, Int. J. Mol. Sci. 23 (22) (2022) 13901, https://doi.org/10.3390/ijms232213901.
[45] M.A. Altamirano-Lozano, L. Alvarez-Barrera, R.A. Mateos-Nava, T.I. Fortoul, J. J. Rodriguez-Mercado, Potential for genotoxic and reprotoxic effects of vanadium compounds due to occupational and environmental exposures: An article based on a presentation at the 8th International Symposium on Vanadium Chemistry, Biological Chemistry, and Toxicology, Washington DC, August 15–18, 2012, J. Immunotoxicol. 11 (1) (2014) 19–27, https://doi.org/10.3109/1547691X.2013.791734.
[46] I. Zwolak, H. Zaporowska, Vanadium carcinogenic, immunotoxic and neurotoxic effects: a review of in vitro studies, J. Appl. Toxicol. 34 (9) (2014) 1025–1037, https://doi.org/10.1002/jat.2997.
[47] D.B. McGregor, Carcinogenicity classification of vanadium pentoxide and inorganic vanadium compounds, the NTP study of carcinogenicity of inhaled vanadium pentoxide, and vanadium chemistry, Regul. Toxicol. Pharmacol. 47 (1) (2007) 110–114, https://doi.org/10.1016/j.yrtph.2006.08.006.
[48] S.K. Ghosh, R. Saha, B. Saha, Toxicity of inorganic vanadium compounds, Res. Chem. Intermed. 41 (2015) 4873–4897, https://doi.org/10.1007/s11164-014-1573-1.
[49] A. Leonard, G.B. Gerber, Mutagenicity, carcinogenicity and teratogenicity of vanadium compounds, Mutat. Res. 317 (1) (1994) 81–88, https://doi.org/10.1016/0165-1110(94)90013-2.
[50] T.B. Starr, J.A. Macgregor, K.D. Ehman, A.I. Nikiforov, Vanadium pentoxide: use of relevant historical control data shows no evidence for a carcinogenic response in F344/N rats, Regul. Toxicol. Pharmacol. 64 (1) (2012) 155–160, https://doi.org/10.1016/j.yrtph.2012.06.017.
[51] T.B. Starr, J.A. MacGregor, Vanadium pentoxide: Risk assessment implications of a treatment-but not dose-related tumorigenic response in B6C3F1 mice, Regul. Toxicol. Pharmacol. 69 (3) (2014) 333–337, https://doi.org/10.1016/j.yrtph.2014.04.013.
[52] M.K. Islam, C. Tsuboya, H. Kusaka, S.I. Aizawa, T. Ueki, H. Michibata, K. Kanamori, Reduction of vanadium (V) to vanadium (IV) by NADPH, and vanadium (IV) to vanadium (III) by cysteine methyl ester in the presence of biologically relevant ligands, Biochim. Et. Biophys. Acta (BBA)-General. Subj. 1770 (8) (2007) 1212–1218, https://doi.org/10.1016/j.bbagen.2007.05.003.
[53] Z. Zhang, C. Huang, J. Li, S.S. Leonard, R. Lanciotti, L. Butterworth, X. Shi, Vanadate-induced cell growth regulation and the role of reactive oxygen species, Arch. Biochem. Biophys. 392 (2) (2001) 311–320, https://doi.org/10.1006/abbi.2001.2464.
[54] V.A. Alcántara-Mejía, J.J. Rodríguez-Mercado, R.A. Mateos-Nava, L. Álvarez-Barrera, E. Santiago-Osorio, E. Bonilla-González, M.A. Altamirano-Lozano, Oxidative damage and cell cycle delay induced by vanadium(III) in human peripheral blood cells, Toxicol. Rep. 13 (2024) 101695, https://doi.org/10.1016/j.toxrep.2024.101695.
[55] J. Escutia-Martínez, E.Y. Hernández-Cruz, K.A. Avendaño-Briseño, J. Pedraza-Chaverri, Vanadium toxicity and mitochondrial dysfunction: Health effects assessment, Caenorhabditis elegans as an emerging model, and the role of plant metabolites, Clin. Bioenerg. 1 (1) (2025) 7, https://doi.org/10.3390/clinbioenerg1010007.
[56] X. He, M.R. Smith, Z.R. Jarrell, V.T. Ly, Y. Liang, C.M. Lee, M. Orr, Y.M. Go, D. P. Jones, Metabolic alterations and mitochondrial dysfunction in human airway BEAS-2B cells exposed to vanadium pentoxide, Toxicology 504 (2024) 153772, https://doi.org/10.1016/j.tox.2024.153772.
[57] I. Zwolak, Protective Effects of dietary antioxidants against vanadium-induced toxicity: a review, Oxid. Med. Cell. Longev. 2020 (1) (2020) 1490316, https://doi.org/10.1155/2020/1490316.
[58] A. Ścibior, D. Gołębiowska, A. Adamczyk, I. Niedźwiecka, E. Fornal, The renal effects of vanadate exposure: potential biomarkers and oxidative stress as a mechanism of functional renal disorders—Preliminary studies, BioMed. Res. Int. 2014 (1) (2014) 740105, https://doi.org/10.1155/2014/740105.
[59] Y.Q. Yu, J.Y. Yang, Oral bioaccessibility and health risk assessment of vanadium (IV) and vanadium (V) in a vanadium titanomagnetite mining region by a whole digestive system in-vitro method (WDSM), Chemosphere 215 (2019) 294–304, https://doi.org/10.1016/j.chemosphere.2018.10.042.
[60] A. Ścibior, Ł. Pietrzyk, Z. Plewa, A. Skiba, Vanadium: Risks and possible benefits in the light of a comprehensive overview of its pharmacotoxicological mechanisms and multi-applications with a summary of further research trends, J. Trace Elem. Med. Biol. 61 (2020) 126508, https://doi.org/10.1016/j.jtemb.2020.126508.
[61] K. Wesseling-Perry, Vanadium toxicity and chronic kidney disease: implications in a green new world, Pediatr. Nephrol. 40 (5) (2025) 1501–1503, https://doi.org/10.1007/s00467-024-06603-2.
[62] J.L. Domingo, Vanadium: a review of the reproductive and developmental toxicity, Reprod. Toxicol. 10 (3) (1996) 175–182, https://doi.org/10.1016/0890-6238(96)00019-6.
[63] J. Taylor, Toxicological profile for vanadium. US Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, 2012. https://www.atsdr.cdc.gov/ToxProfiles/tp58-p.pdf (Available at).
[64] B. Lyonnet, Lemploi thérapeutique des derives du vanadium, Presse Med. 1 (1899) 191–192.
[65] L.M.P.F. Amaral, T. Moniz, A.M.N. Silva, M. Rangel, Vanadium compounds with antidiabetic potential, Int. J. Mol. Sci. 24 (21) (2023) 15675, https://doi.org/10.3390/ijms242115675.
[66] K.H. Thompson, C. Orvig, Vanadium in diabetes: 100 years from Phase 0 to Phase I, J. Inorg. Biochem. 100 (12) (2006) 1925–1935, https://doi.org/10.1016/j.jinorgbio.2006.09.038.
[67] Y. Shechter, S.J.D. Karlish, Insulin-like stimulation of glucose oxidation in rat adipocytes by vanadyl (IV) ions, Nature 284 (5756) (1980) 556–558, https://doi.org/10.1038/284556a0.
[68] S.S. Abdelsalam, H.M. Korashy, A. Zeidan, A. Agouni, The role of protein tyrosine phosphatase (PTP)-1B in cardiovascular disease and its interplay with insulin resistance, Biomolecules 9 (7) (2019) 286, https://doi.org/10.3390/biom9070286.

[69] L. Zhang, Y. Liu, X. Li, J. Zheng, G. Yang, G. Zhao, R. Su, Inhibition of protein tyrosine phosphatase 1B and alkaline phosphatase by bis(maltolato)oxovanadium (IV), J. Inorg. Biochem. 102 (8) (2008) 1731–1738, https://doi.org/10.1016/j.jinorgbio.2008.04.019.
[70] T. Behl, A. Gupta, A. Sehgal, A. Albarrati, M. Albratty, A.M. Meraya, A. Najmi, S. Bhatia, S. Bungau, Exploring protein tyrosine phosphatases (PTP) and PTP-1B inhibitors in management of diabetes mellitus, Biomed. Pharmacother. 153 (2022) 113405, https://doi.org/10.1016/j.biopha.2022.113405.
[71] E. Irving, A.W. Stoker, Vanadium compounds as PTP inhibitors, Molecules 22 (12) (2017) 2269, https://doi.org/10.3390/molecules22122269.
[72] K.H. Thompson, J. Lichter, C. LeBel, M.C. Scaife, J.H. McNeill, C. Orvig, Vanadium treatment of type 2 diabetes: a view to the future, J. Inorg. Biochem. 103 (4) (2009) 554–568, https://doi.org/10.1016/j.jinorgbio.2008.12.003.
[73] F. Ghalichi, A. Ostadrahimi, M. Saghafi-Asl, Vanadium and diabetic dyslipidemia: a systematic review of animal studies, J. Trace Elem. Med. Biol. 71 (2022) 126955, https://doi.org/10.1016/j.jtemb.2022.126955.
[74] M. Soveid, G.A. Dehghani, G.R. Omrani, Long-term efficacy and safety of vanadium in the treatment of type 1 diabetes, Arch. Iran. Med. 16 (7) (2013) 408–411. PMID: 23808778.
[75] J.L. Domingo, M. Gómez, D.J. Sánchez, J.M. Llobet, C.L. Keen, Toxicology of vanadium compounds in diabetic rats: the action of chelating agents on vanadium accumulation, Mol. Cell. Biochem. 153 (1–2) (1995) 233–240, https://doi.org/10.1007/BF01075942.
[76] T. Scior, J.A. Guevara-Garcia, Q.T. Do, P. Bernard, S. Laufer, Why antidiabetic vanadium complexes are not in the pipeline of "Big Pharma" drug research? A critical review, Curr. Med. Chem. 23 (25) (2016) 2874–2891, https://doi.org/10.2174/0929867323666160321121138.
[77] J. Yang, M. Wang, Y. Jia, M. Gou, J. Zeyer, Toxicity of vanadium in soil on soybean at different growth stages, Environ. Pollut. 231 (1) (2017) 48–58, https://doi.org/10.1016/j.envpol.2017.07.075.
[78] S. Li, S.G. Nielsen, J.D. Owens, Global cycling of vanadium isotopes from multiple ocean water masses and a restricted euxinic basin, Geochim. Et. Cosmochim. Acta 409 (2025) 82–92, https://doi.org/10.1016/j.gca.2025.08.037.
[79] H.R. Pan, H.F. Hsu, Vanadium Catalysis Relevant to Nitrogenase, in: M. Sutradhar, A.J.L. Pombeiro, J.A.L. da Silva (Eds.), Vanadium Catalysis, Royal Society of Chemistry, UK, 2020, https://doi.org/10.1039/9781839160882-00564.
[80] M.A. Manzoor, I.A. Sabir, I.H. Shah, M. Azam, M. Usman, M.S. Malik, A. Rehman, A. Rehman, G. Murtaza, M. Khalid, G. Saleem, M.T. Manzoor, C. Song, Vanadium in soil-plant systems: uptake mechanisms, ecotoxicological impacts, and microbial remediation strategies, Land. Degrad. Dev. 37 (10) (2026) 4472–4495, https://doi.org/10.1002/ldr.70401.
[81] Q. Zou, Y. Gao, S. Yi, J. Jiang, A. Aihemaiti, D. Li, M. Yang, Multi-step column leaching using low-molecular-weight organic acids for remediating vanadium- and chromium-contaminated soil, Environ. Sci. Pollut. Res. 26 (15) (2019) 15406–15413, https://doi.org/10.1007/s11356-019-04915-7.
[82] Y. Dong, H. Lin, Y. Zhao, E.R.G.Y. Menzembere, Remediation of vanadium-contaminated soils by the combination of natural clay mineral and humic acid, J. Clean. Prod. 279 (2021) 123874, https://doi.org/10.1016/j.jclepro.2020.123874.
[83] M.R. Haak, S.P. Indraratne, Soil amendments for vanadium remediation: a review of remediation of vanadium in soil through chemical stabilization and bioremediation, Environ. Geochem. Health 45 (7) (2023) 4107–4125, https://doi.org/10.1007/s10653-023-01498-8.
[84] J. He, B. Zhang, Y. Wang, H. Liu, W. Yan, A.G. Borthwick, Y. Feng, Vanadate bio-detoxification driven by pyrrhotite with secondary mineral formation, Environ. Sci. Technol. 57 (4) (2023) 1807–1818, https://doi.org/10.1021/acs.est.2c06184.
[85] A. Aihemaiti, J. Jiang, D. Li, N. Liu, M. Yang, Y. Meng, Q. Zou, Toxic metal tolerance in native plant species grown in a vanadium mining area, Environ. Sci. Pollut. Res. Int. 24 (34) (2017) 26839–26850, https://doi.org/10.1007/s11356-017-0250-5.
[86] Z. Long, H. Bing, H. Zhu, Y. Wu, Divergent phytoaccumulation mechanisms of vanadium and cadmium by native plants in a 51-year-restored legacy vanadium-titanium magnetite tailings pond, J. Environ. Sci. (Press.) (2026), https://doi.org/10.1016/j.jes.2026.01.007.
[87] L. Hao, H. Zhou, Z. Zhao, J. Zhang, B. Fu, X. Hao, Enhanced phytoremediation of vanadium using coffee grounds and fast-growing plants: Integrating machine learning for predictive modeling, J. Environ. Manag. 370 (2024) 122747, https://doi.org/10.1016/j.jenvman.2024.122747.
[88] X. Kang, Y. Cui, L. Zeng, Z. Tian, Y. Xu, Q. Chen, G.M. Gadd, X. Leng, X. Yu, Assembly processes and ecological dynamics of root-associated bacterial communities during phytoremediation of vanadium-titanium mine tailings using Millettia pinnata, Rhizosphere 29 (2024) 100837, https://doi.org/10.1016/j.rhisph.2023.100837.
[89] F.L. Li, Y. Qiu, X. Xu, F. Yang, Z. Wang, J. Feng, J. Wang, EDTA-enhanced phytoremediation of heavy metals from sludge soil by Italian ryegrass (Lolium perenne L.), Ecotoxicol. Environ. Saf. 191 (2020) 110185, https://doi.org/10.1016/j.ecoenv.2020.110185.
[90] L. Zeng, Z. Tian, X. Kang, Y. Xu, B. Zhao, Q. Chen, Y. Gu, Q. Xiang, K. Zhao, L. Zou, M. Ma, P. Pentinnen, X. Yu, Bacterial community drives soil organic carbon transformation in vanadium titanium magnetite tailings through remediation using Pongamia pinnata, J. Environ. Manag. 360 (2024) 121156, https://doi.org/10.1016/j.jenvman.2024.121156.
[91] R. Qiu, B. Zhang, J. Li, Q. Lv, S. Wang, Q. Gu, Enhanced vanadium (V) reduction and bioelectricity generation in microbial fuel cells with biocathode, J. Power Sources 359 (2017) 379–383, https://doi.org/10.1016/j.jpowsour.2017.05.099.
[92] L. Wang, S. Chen, R. Li, B. Zhang, Novel metabolic pathways of bioelectrochemical vanadate reduction by Thiobacillus denitrificans without exogenous electron donor supplementation in groundwater, Water Res. 282 (2025) 123739, https://doi.org/10.1016/j.watres.2025.123739.
[93] WHO (World Health Organization), Guidelines for Drinking-water Quality. incorporating the 1st addendum, 4th edition, World Health Organization, Geneva, 2017. https://www.who.int/publications/i/item/9789241549950 (Available at).
[94] EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), Opinion of the scientific panel on dietetic products, nutrition and allergies related to the tolerable upper intake level of vanadium, EFSA J. 2 (3) (2004) 33, https://doi.org/10.2903/j.efsa.2004.33.
[95] J.M. Llobet, J.L. Domingo, Acute toxicity of vanadium compounds in rats and mice, Toxicol. Lett. 23 (2) (1984) 227–231, https://doi.org/10.1016/0378-4274(84)90131-0.
[96] Y. Zhao, T. Ramachandran, A. Ghosh, A.G. Al-Sehemi, Y.A. Kumar, S.S. Rao, A. K. Yadav, D. Mani, Unlocking the potential of vanadium redox flow batteries: recent advances in biomass lignin-based carbon fibers and future outlook, Biomass. Bioenergy 200 (2025) 108052, https://doi.org/10.1016/j.biombioe.2025.108052.
[97] J.C. Pessoa, S. Etcheverry, D. Gambino, Vanadium compounds in medicine, Coord. Chem. Rev. 301 (2015) 24–48, https://doi.org/10.1016/j.ccr.2014.12.002.
[98] S. Selvaraj, U.M. Krishnan, Vanadium–flavonoid complexes: a promising class of molecules for therapeutic applications, J. Med. Chem. 64 (17) (2021) 12435–12452, https://doi.org/10.1021/acs.jmedchem.1c00405.
[99] S. Treviño, A. Díaz, E. Sánchez-Lara, B.L. Sanchez-Gaytan, J.M. Perez-Aguilar, E. González-Vergara, Vanadium in biological action: chemical, pharmacological aspects, and metabolic implications in diabetes mellitus, Biol. Trace Elem. Res. 188 (1) (2019) 68–98, https://doi.org/10.1007/s12011-018-1540-6.
[100] V.A. Ferretti, I.E. León, An overview of vanadium and cell signaling in potential cancer treatments, Inorganics 10 (4) (2022) 47, https://doi.org/10.3390/inorganics10040047.
[101] B. Zhang, H. Zhang, J. He, S. Zhou, H. Dong, J. Rinklebe, Y.S. Ok, Vanadium in the environment: biogeochemistry and bioremediation, Environ. Sci. Technol. 57 (39) (2023) 14770–14786, https://doi.org/10.1021/acs.est.3c04508.