

# Tungsten Contamination of Soils and Sediments: Current State of Science

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**Abstract** Tungsten (W) is commonly employed as a non-toxic alternative to lead in a broad variety of industrial and military applications. However, correlations between environmental contamination through soil, water and airborne pathways, and biological effects such as epithelial damage, bioaccumulation, and trophic mobility, have led to its classification as an “emerging contaminant.” Of particular concern are recent clusters of childhood leukemia and lung cancer in the vicinity of tungsten mines and processing facilities. High environmental tungsten availability has also been associated with altered thyroid function, cardiovascular disease, and prolonged elevation of concentrations in blood, breath, and urine. Tungsten’s use as a replacement for lead (Pb) in military munitions has resulted in leaching of tungsten into soil and into soft tissues in which bullet fragments are embedded. Despite these associations, no consensus has been reached regarding the mechanisms by which tungsten affects the human body. Particularly confounding are the issues of co-toxicity with other known contaminants such as arsenic, cobalt, and cadmium, and differences resulting from the various methods of ingestion. The present paper summarizes the current behavior of tungsten in the environment, its occurrence within the pedosphere, biosphere, and atmosphere, and discusses its potential effects on exposed biota (especially humans). In

particular, knowledge gaps are identified regarding the biological mechanisms of tungsten-related disease, which urgently require further elucidation in order to develop appropriate policies and management practices for the use of this element.

**Keywords** Tungsten · Sediments · Hydrochemistry · Contamination · Bioavailability

## Introduction

Tungsten (W) has been identified as an “emerging contaminant” by the Environmental Protection Agency (EPA) [1], that is; a contaminant whose presence within or threat to the environment has only recently been identified [2]. Whereas W has long been presumed as a non-toxic alternative to lead (Pb) for industrial, military, and medical applications [3], recent research questions the environmental safety of this element. Due to the limited understanding of the extent, phases, mobility, and mode-of-action of W, there exist very few regulations pertaining to it compared to more well-known contaminants. The present review examines the sources, uses, behavior, and toxicity of W, within the various environmental spheres (i.e., the pedosphere, biosphere, hydrosphere, and atmosphere).

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## Natural Occurrence of Tungsten

Tungsten is a transition element in group VI, refractory metal, which bears many similarities to its neighboring element: molybdenum (Mo) [4] with which W commonly co-occurs [5, 6]. In the natural environment, W occurs within igneous [7] and metamorphic rocks [8], and is commonly associated with hydrothermal processes leading to the formation of ore deposits [9]. Common ores include scheelite and hubernite-wolframite-

ferberite [10], the weathering of which releases W to form various compounds and oxidative states. These range from  $W^{2-}$  to  $W^{6+}$ , with the 6+ valence state being the most stable in waters. Tungsten mineral ore formations are commonly found in Phanerozoic fold belts and zones of tectonic-magmatic activation of ancient consolidated structures of the crust [11]. The largest concentrations of tungsten ores are found in south-east China and the Republic of Korea, eastern Mongolia and Transbaikalia, Kazakhstan, the south Tien Shan, north Caucasus, central Europe, Canada, eastern Australia, and Tasmania [12]. China is by far the greatest producer and consumer of W, and is estimated to hold the largest ore reserves [12]. Regarding the dominant W ore types, Wolframite deposits are typically associated with acidic, Ca-poor granitoids and high-temperature quartz veins and greisen, whereas scheelite is commonly associated with granodioritic to monzonitic rocks. Tungsten is typically extracted from these ores in the form of tungstate ( $WO_4^{2-}$ ).

### Uses of Tungsten

Tungsten is a widely used resource in industrial and manufacturing applications due to its high density and tensile strength [3, 12]. Cemented tungsten carbide accounts for approximately 60% of the US tungsten production [12]. Tungsten carbide is used to make a range of items including high-speed tools, knives, building materials, jet engine turbines, radiation shields, jewelry, and light bulb filaments, and as a perceived safe alternative to Pb in ammunition and recreational fishing weights [12, 13]. As such, it has become ubiquitous throughout various environmental spheres as a result of industrial applications, beyond its natural lithological origin. Occurrence of W within the Earth's crust is estimated as  $1.5 \text{ mg kg}^{-1}$  [14]. The natural concentration of W in wolframite and scheelite ores may vary substantially depending on the temperature and chemical composition during ore formation [7]. While most mineral ores contain <1% W, concentrations in wolframite and scheelite range between 60 and 64% by weight. Tungsten must therefore be extracted from these ore minerals or from scrap metals (in which concentrations reach 40–95%) [15] using a variety of industrial processes including solvent extraction, and pressure and heat treatments [15, 16]. The recovery rate and purity of tungsten differ between extraction methods and are of economic importance within the metallurgical industry [16]. Mining of tungsten ores can result in the introduction of contaminated soil, wash, and leachate into the environment [17, 18]. Until relatively recently, there has been minimal recognition of potentially negative environmental consequences of W mining and processing; hence, there is comparatively little legislation pertaining to its environmental quality indicators and thresholds relative to other metals and metalloids (e.g., Pb, As). Recovery from scrap metals has represented an increasing proportion of total W production from 2010 to the present; however, total ore extraction has also increased,

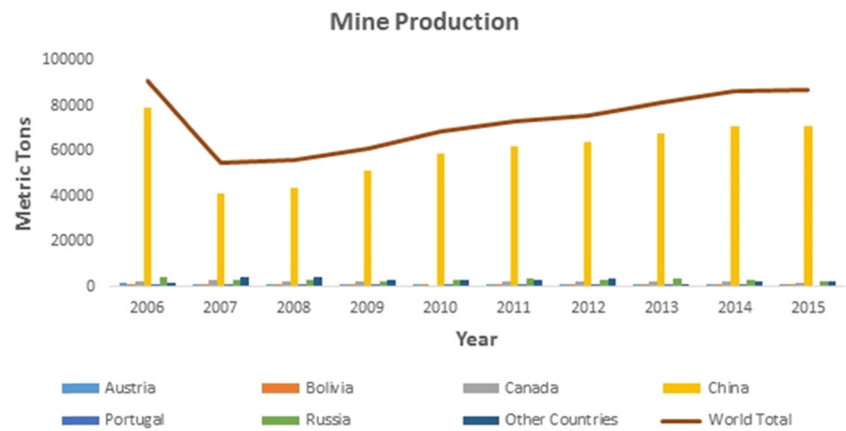
particularly in Asia (Fig. 1) [12, 19–27]. As an “emergent contaminant,” and because of the trend of increasing world production, it seems likely that this metal will garner increasing attention over the coming years [28].

### Tungsten in the Pedosphere

Whereas the baseline concentration of W in non-contaminated soil typically ranges from 0.4 to  $5 \text{ mg kg}^{-1}$  [29], accumulation can occur as a result of human activity. Considering such activities as the major W source in the environment, soil represents both a sink and a medium through which W may be transported to groundwater via leaching. In soil, metallic and other species of W introduced to the system undergo oxidative dissolution, forming tungstate anion ( $WO_4^{2-}$ ). Furthermore, prolonged residence times (which may occur as a result of low soil moisture) lead to increased soluble W in leachate as a result of greater oxidation over time [30]. Soil pH has been observed to decrease (from 6.7 to 5.2 pH) resulting from the oxidation of W [30]. That study also demonstrated the formation of a variety of polytungstate species, dependent upon soil chemistry, which exhibit unique residence times. In general, monomeric tungstate species (i.e.,  $WO_4^{2-}$ ) predominate in alkaline soils, whereas polymeric tungstates (polytungstate) species are more common in acidic soils. The timescales, quantity, and risk of W transport are therefore dictated not only by the properties of the element but also by soil characteristics including texture, density, and moisture content. Soil pH has been found to exert a strong control on W mobility [31]. Similarly, to arsenic (As), W mobility is lower under acidic conditions due to increased sorption in low-pH soils [31, 32]. Lysimeter transport studies on peat and clay soils demonstrated high retention of W in upper soil layers, which declined with depth [32]. Adsorption curves were developed using Freundlich and Langmuir isotherms for both mono and metatungstates [33–37]. Adsorption affinity of clays and Pahokee peat for monotungstates follows the order: Pahokee peat > kaolinite > montmorillonite > illite. For metatungstates, it is as follows: kaolinite > Pahokee peat > montmorillonite > illite [32]. Hence, in addition to W speciation and soil pH, charges of the clay mineral surface should be considered as a contributing factor for W adsorption.

As a result of its complex sorption and speciation behavior, quantifying W concentrations within the soil can be challenging. Due to the complex chemistry of W, traditional acid digestion does not extract W that could become mobile under normal environmental conditions [38]. This is primarily due to the precipitation of insoluble tungstates or the adsorption of tungstates onto soil particles and sediments. One effective

**Fig. 1** Annual mine production (tons) of W ore (selected countries). Adapted from USGS mineral surveys 2007–2015 [19–27]



procedure capitalizes on W's ability to polymerize with an oxyanion acid to yield acid soluble W species for measurement by ICP-AES or ICP-MS, while simultaneously allowing determination of other metals extracted during digestion. The procedure involves the addition of phosphoric acid to a standard nitric acid and hydrogen peroxide digestion to promote W solubilization. This method shows great efficiency relative to other standard procedures, with minor differences in other metal recoveries [38].

Mining of tungstate ores represents a major source for W introduction to the pedosphere. Environmental impact studies have therefore focused on regions geographically close to mining and processing sites. A UK study [17] examined and compared elemental concentrations of As, Cu, Zn, and W in plant (*Calluna*, *Agrostis*, and *Sphagnum*) and of spoil samples from a wolframite mining wash site. Despite decommissioning of the mine almost 100 years prior to the study, there were high concentrations of W (944–1637 mg kg<sup>-1</sup> average) and As (2962–4227 mg kg<sup>-1</sup> average) at four sampling locations near (<300 m) the mine entrance in the soil samples. This prolonged time lag of W through the pedosphere enables transfer of W by plants (via true plant uptake or surface contamination) over many decades and suggests a potential for W to be incorporated through the trophic levels. Hence, a holistic view of the source-pathway-receptor relationship is necessary when assessing W in natural environments.

In a study by Lin et al. [39], they demonstrate that in areas closed to 100s of years of W mining activity, significantly elevated W concentrations in the soil adjacent to the W mines were substantiated. Even among the crops grown on the soils, the rice uptake of W shows a linear dependence of W contents in the rice root, stem, leaf, and grain on the soil W content and the different chemical forms. In the same study, it also shows that the enrichment factor of W decreased in the order from the root to leaf to stem and to grain in the rice.

A relatively modern vector by which W may be introduced to the environment is from military munitions, in which W was mooted as a possible Pb alternative in the US Army Green

Ammunition program [40]. This was originally conceived as a way to limit the addition of toxic Pb to the environment by replacement with what was thought to be a non-toxic, inert metal of low environmental mobility [13, 30]. Consequently, soil contamination as a result of military W use has also been documented. Three small arms ranges at Camp Edwards in Massachusetts, USA, were investigated in relation to potential environmental W contamination resulting from the discharge of W munitions over <6 years [40]. Soil testing revealed that range soils exhibited high W concentrations in the upper 25 cm (up to 2080 mg kg<sup>-1</sup>) which decreased down the soil profile by an order of magnitude approximately every 25 cm. These concentrations were localized but extremely high; comparative measures from off-site locations reported concentrations of only 1.3 mg kg<sup>-1</sup>. Examination of groundwater extracted from a 30-m deep well showed W concentrations of <0.56 mg L<sup>-1</sup>. In agreement with the prior study, it has been determined that mobilization of W was the greatest in sandy, slightly acidic, and aerobic soils [30, 41]. The greatly decreased concentrations along the soil profiles suggest (in agreement with [32]) a long biogeochemical time lag as a result of strong adsorption; however, the cumulative leaching of W over a broad area may still result in elevated concentrations at an abstraction point, as observed from the groundwater samples [40].

Contamination over time of silty sand, sandy clay, and silt soils by W shot was examined using mesoscale rainfall lysimeters [42]. Leachate, runoff, and soil samples were analyzed using scanning electron microscopy (SEM). The SEM results showed that the soil's particle size initially affected the amount of metal that was sheared off on impact; greatest shearing occurred in soils with the largest particle size (sand < silt < clay). Consequently, increased shearing promoted increased dissolution and may lead to the introduction of greater W concentrations in combat theaters exhibiting coarse soil types. One must consider that the nature of specific munitions may confer different propensities for shearing, although no studies on this are known to the authors of this review.

## Tungsten in the Hydrosphere

As with many environmental contaminants, water plays a crucial role in the distribution and delivery of W compounds. There are several factors that influence groundwater W concentration including aquifer recharge from surface waters exhibiting elevated W concentrations, the dissolution or desorption of W from minerals or sediments within an aquifer (either as a result of groundwater Fe content or pH), and incursion of W enriched hydrothermal fluids [43]. These are in addition to the anthropogenic factors mentioned previously. The predominance of these factors differs; Seiler et al. [43] attributed elevated W concentrations in western Nevada and eastern California to hydrothermal mixing, whereas Johannesson et al. [31] identified large increases in W concentration (from 1.9 to 1297 pmol kg<sup>-1</sup>) along the Carrizo Sand aquifer (Texas), as a result of desorption as pH increased from 6.2 to 8.5 along the flowpath. The Aquia aquifer in Maryland did not exceed a pH of 8.4 and exhibited a smaller range in W concentration fluctuations (from 6.5 to 184 pmol kg<sup>-1</sup>). The tungstate oxyanion, WO<sub>4</sub><sup>2-</sup>, is the dominant form in natural waters. Although monotungstates are dominant, W can polymerize under acidic conditions. Once formed, polytungstates may persist in the environment over a wide range of pH [30, 41, 44], and they have a much more toxic effect on flora and fauna compared to monotungstates [45, 46]. Although stability constants of thiotungstate species are about two orders of magnitude less than those of their molybdate counterparts, the elevated W concentrations observed in sulfidic waters (high S(-II)) may be attributed to formation of thiotungstate species [31, 46–49]. In this scenario, low dissolved S(-II) concentrations and the occurrence of aquifer sediment with higher Fe(III) oxide/oxyhydroxide contents indicated a buffering effect on W dissolution, leading to more stable concentrations [31].

In a study by Mohajerin et al. [47], equilibrium constants for thiotungstates were used to examine tungstate speciation in sulfidic waters. Preliminary field investigations indicated that thiotungstate formation may lead to increased W solubility and modeling indicated that increasing dissolved sulfide concentrations and decreasing pH are favorable for thiotungstate formation. It was predicted that thiotungstate species are negligible in most natural waters, but are likely to be important in circum-neutral, anoxic waters with 0.1-mM S(-II) concentrations. Natural sulfidic waters that are conducive to thiotungstate formation include the Black Sea, and Tyro and Bannock basins, and soil pore-waters exhibiting high rates of sulfate reduction are also common in salt marshes. Such locations may have potential to offset elevated W concentrations resulting from the disposal of industrial effluent, and also natural scavenging of W from within sulfidic waters in environments (like in salt marshes) may help in reducing the bioavailability of W [47].

A 2008 study examined adsorption as a control on W in groundwater using laboratory experiments and an example from Fallon, Nevada [30]. Geochemical modeling of W predicted that adsorption is the main control on the concentration of W in Fallon groundwater. Changes in pH can release W from solid to dissolved phases, resulting in spikes in groundwater concentrations. However, the authors recommend further study to identify the speciation of remaining W in the sediment, as well as to investigate its mobility in relation to changing conditions of the aquifer. Similar conclusions have been reached in other studies [43]. In another example, a small flooded scheelite skarn deposit in remote southwest Montana, USA, was examined. The current lake at this site had formerly been an open-pit mine, which was decommissioned in the 1970s. With almost neutral pH, very low nutrients, sulfates, and most metals (including W), the authors state that the lack of W in this lake is likely a result of sorption or the limited availability of scheelite due to its extraction during mining processes in the past [50]. It cannot therefore be assumed that rock-type alone may dictate W concentrations at any stage of the hydrologic system, and a more comprehensive approach to site characterization is essential.

In a study by Torres et al. [51] formulated within natural aquatic systems, they show that at neutral and basic pH values, ionic pair species such as [Ca (WO<sub>4</sub>)] are formed to high extents, where dissolved W is high to start with, which concludes that tungsten anions are in general more basic and form stronger associations with metal cations (such as Ca<sup>2+</sup>). For the acidic pH range, polyoxoanion associations with cations are also found mostly relevant for tungsten (VI) where W concentrations are generally of the natural waters.

## Tungsten in the Atmosphere

The production of dust from industrial sources has allowed, in recent years, atmospheric transport to become a vector for the spread of W [52], and is suspected to be a burgeoning cause of health problems to humans via inhalation [52–55]. The size of airborne particles has been assessed using automated electron microprobe and wavelength-dispersive spectrometry as well as transmission electron microscopy [56]. Particles of W ranged in size from 1 to 5.9 nm in diameter, and it was found that the size and concentration of these particles decreased with distance from a W processing factory. Assessment of airborne W deposition was conducted in the town of Fallon, Nevada [57], by collecting samples of lichen and their substrates from within Fallon and from four different rock outcrops in each of the cardinal directions, all of which were located at least 20 km away from central Fallon. It was found that in the lichens themselves, W (and Co) concentrations were significantly higher within Fallon compared to those in the control sites outside of the town. The substrates of the

lichens showed no difference, indicating that airborne deposition was the likely vector. It is estimated that the source of the W dust is not indigenous to Fallon, but rather, is a byproduct of a hard-metal facility located within the town [56–58]. That study was conducted in relation to suspected relationships between airborne W and Co dust and a childhood leukemia cluster (discussed later in this review).

High-volume air samplers were used to examine airborne particulates for trace metal content in Fallon and in four other western Nevada towns within 100 km of Fallon [53]. The most notable metal found in Fallon dust was indeed W, followed by Co. The concentration of airborne W was greatly elevated in Fallon (median values of 0.57–8.56 ng m<sup>-3</sup>) relative to that in the other four towns (0.12–0.16 ng m<sup>-3</sup>), and within Fallon concentrations of airborne W and Co co-varied significantly, both temporally and spatially. Even though there is limited regulation specific to W in the natural environment, exposure to W in the workplace is regulated in various ways. Occupational exposure to insoluble W is limited to 5 mg m<sup>-3</sup> of air, soluble W is limited to 1 mg m<sup>-3</sup> of air, dust of cemented W carbide with no more than 2% Co is limited to 0.1 mg W m<sup>-3</sup> of air, and dust of cemented W carbide with no more than 0.3% Ni is limited to 15 µg W m<sup>-3</sup> of air [59].

### Tungsten in the Biosphere

The effects of W contamination on the biosphere have not been fully quantified, although it is suspected that W may have adverse effects on organisms and may increase in significance due to bioaccumulation within the food chain or environment [60]. The lack of mobility of W under acidic soil conditions has been observed to limit bioaccumulation in various plant species, whereas greater bioaccumulation occurred in similarly contaminated alkaline soils [39, 60]. The potential for biotic contamination is therefore dependent not only on the properties of W itself but also on the medium by which it is transported or stored.

A recent study focused on the accumulation of W in rice in an area in close proximity to the world's largest- and longest-operating W mines in the Jiangxi province of southeastern China [39]. The soil, rice root, stem, leaf, and grain samples collected from 15 sites that were adjacent (<11.3 km) to the mines were analyzed for W concentrations and species. The W contents of the soil ranged from 3.99 to 43.7 mg kg<sup>-1</sup>, and contents of W for the roots, stems, leaves, and grains averaged 7.06, 2.34, 4.76, and 0.17 mg kg<sup>-1</sup>, respectively. The researchers of that study highlighted the need for threshold toxicity levels and assessment of chronic exposure to be determined, as residents of that region are liable to ingest up to 0.23 mg day<sup>-1</sup> via contaminated rice [39]. Research by Johnson et al. [61] similarly noted an accumulation of W in the tissue of sunflowers, which was twofold greater in the

roots than that in the leaves. Growth of the sunflowers grown in W-spiked soil showed significant dose-dependent impairment. The study did suggest the use of this species as a bio-remediation measure for the removal of W from contaminated soil, pending further research. Strigul et al. [62] similarly proposed perennial ryegrass as a suitable species for soil remediation.

The effects of sodium tungstate and an aged W powder-spiked soil containing both monomeric and polymeric tungstates were investigated on a cabbage species, *Brassica oleracea*, and a snail species, *Otala lacteal* [60]. Bioassays indicated cabbage growth was impaired at 436 mg kg<sup>-1</sup> in the spiked soil; whereas snail survival was not impacted until soil W content reached 3793 mg kg<sup>-1</sup>. Dermal exposure was also tested; sodium tungstate was more toxic to the snail, with a lethal median concentration of 859 mg of W kg<sup>-1</sup>. The snail significantly bioaccumulated W in its hepatopancreas (86.3 mg kg<sup>-1</sup>). The greatest accumulation of W in cabbage occurred within leaf veins (134 mg kg<sup>-1</sup>), (determined via synchrotron mapping). These results suggest that snails consuming contaminated cabbage accumulated higher W concentrations relative to the accumulation from direct contact with the soil, supporting robust trophic transfer. Synchrotron x-ray fluorescence mapping also showed significant evidence of W deposition in the inner layer of the snail shell. This could suggest the potential use of snail shells as a useful biomonitoring tool for metal contamination [60]. A similar *Otala lacteal* study [63] examined W alteration of biomechanical properties in snail shell through the use of nanomechanical experiments. It was determined that the biomineralization of the snail shell is affected by the presence of W, including a >50% reduction in mechanical properties of the shells (hardness and indentation modulus).

An earthworm species—*Eisenia fetida* (redworm)—has been used in several studies on W toxicity in soil invertebrates. Inouye et al. [64] examined the survival, growth, and reproduction of redworms exposed to W. Comparative studies with Pb as a reference toxicant were also performed. Results show the halt of reproduction occurred at a lower concentration of W (704 mg kg<sup>-1</sup>) compared to that of Pb, which reduced reproduction but did not halt it entirely even at the highest treatment of 1650 mg kg<sup>-1</sup>. The sublethal toxicity of W may, therefore, be greater than that of Pb, which may have historically contributed to the perception that W was a safe alternative to Pb, due to more subtle toxicant effects. Conversely, Bamford et al. [65] reported no effect on mortality or reproduction of redworms exposed to soil W concentrations of 1000 or 586 mg kg<sup>-1</sup>, as sodium tungstate or tungsten, respectively. The authors of that study suggested that the effects observed by Inouye et al. [64] may have been as a result of co-exposure to Pb, which was present in that study at 5.8 mg kg<sup>-1</sup> whereas this concentration of Pb alone was shown to be insufficient to impair reproduction; further

examination is required to ascertain whether simultaneous exposure to sublethal levels of W and Pb may have an amplified effect on mortality and reproduction. To this end, Inouye et al. [64] recommended further study in this field and on other invertebrates.

A further study of particulate and soluble W in soil observed the death of redworms, plant species, and a substantial portion of the bacterial component and an increase of the fungal biomass, when W concentrations exceeded 1% on a mass basis (10,000 ppm). These effects are hypothesized to be related to the soil acidification during the W dissolution, and by uptake of W ions by biota as W enrichment of the rhizosphere occurs [62]. Whereas such high concentrations are rarely found in uncontaminated soil, anthropogenic activities such as mining [17] have led to some instances of these concentrations. In the latter study [17], bioaccumulation of W by plants grown in highly contaminated soil was observed within different tissues of *Calluna vulgaris* (a heather species). The highest concentration of W was observed in root tissues ( $655 \text{ mg kg}^{-1}$ ), compared to that in the stems ( $48.9 \text{ mg kg}^{-1}$ ) or foliage ( $124 \text{ mg kg}^{-1}$ ). Although it is difficult to judge whether the cleaning procedure adopted was sufficient to completely remove surface contamination of plant materials by soil/dust, this is consistent with the hypothesis of W uptake through the plant roots from the contaminated soil at that site, rather than deposition of airborne particles, as in other scenarios [66].

Comparison of the toxicity of mono and polytungstates has been conducted on a species of fish: *Poecilia reticulata* [45]. LD<sub>50</sub> values for 1–14 days showed that sodium metatungstate (poly) was significantly more toxic to fish (LD<sub>50</sub>  $0.86\text{--}3.88 \text{ g L}^{-1}$ ) than sodium tungstate (mono) (LD<sub>50</sub>  $0.13\text{--}0.85 \text{ g L}^{-1}$ ), which could be classified as having low toxicity to fish. The mechanisms of toxicity of these tungstate species are uncertain, but it is suggested that the mechanisms are related to epithelial damage [45, 62]. This is in agreement with the observations of Kühnel et al. [67] on rainbow trout (*Oncorhynchus mykiss*). Speciation of W, such as that which occurs during transport through the soil to a waterbody, or in waterbodies themselves [48], can therefore influence the level of toxicity exhibited on receptor ecology and should be considered in environmental assessments, rather than reliance on gross W contents alone.

In 2014, the toxicity potentials of various concentrations (0–1000 ppm) of  $\text{WO}_4^{2-}$  nano-particles (<100 nm) were investigated in cultured primary rat hepatocytes [68]. Higher concentrations (300, 500, and  $1000 \text{ mg kg}^{-1}$ ) caused significant ( $p < 0.05$ ) decreases of cell viability due to impaired mitochondrial function as a result of oxidative damage. These results are of particular interest due to the increasing use of tungsten oxide nano-particles in manufacturing semiconducting materials, optics, and various mechanochemical applications. Oxidative stress has been reported as a general

mechanism causing inflammatory diseases and cancer [69]; this may indicate a possible method of W toxicity in humans [70].

### Effects of Tungsten on Humans

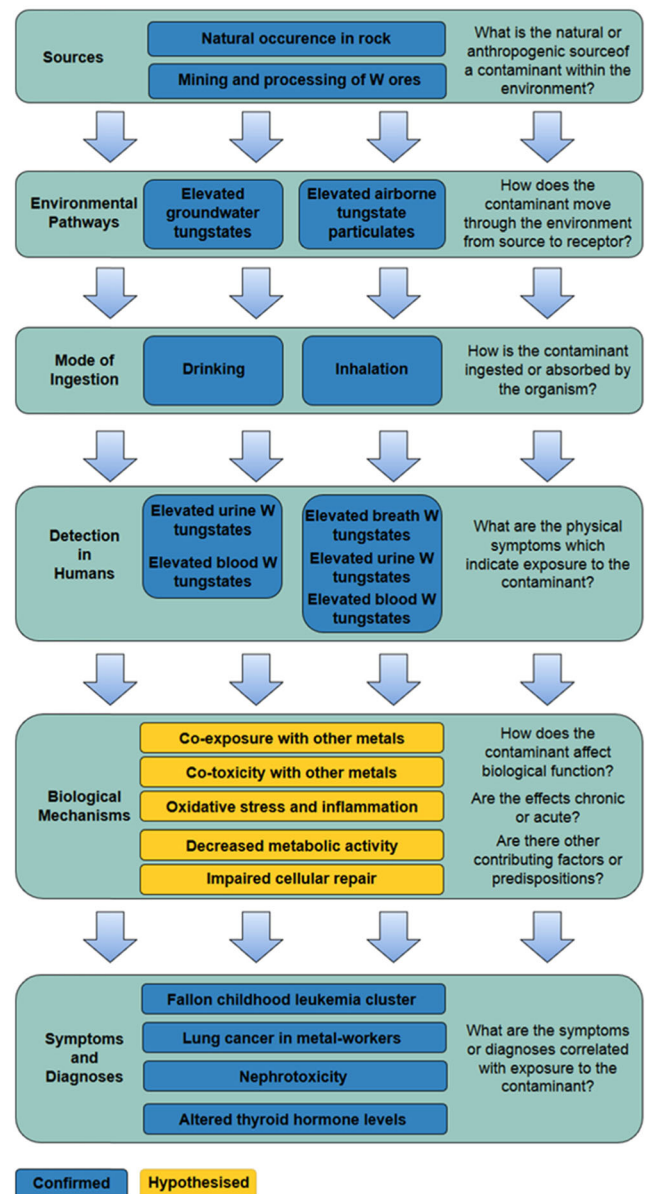
Western Nevada, USA, has become a focal point for many W studies [52, 53, 56–58, 71–73] as a result of 16 cases of acute childhood leukemia among a small population (c. 8000 total residents/<2500 children) within the town of Fallon. The United States Center of Disease Control (CDC) found that approximately 68% of the inhabitants tested in the metalloregion were in excess of the 95th percentile for concentrations of W in their urine [74]; however, no difference was observed in urine concentrations of families in which leukemia has been diagnosed, and those in which it had not. Children in the Fallon region exhibited mean urine W of 2.31 ppb [75], compared to typical ranges of 0.08–0.7 ppb among the general population [75]. A study focusing on inhalation of tungsten carbide cobalt (WC-Co) dust and its effects on lung epithelial cells when dosed with micro- (4  $\mu\text{m}$ ) and nano- (80 nm) sized particles over variable time showed that nano-particles exhibited significantly higher toxicity at lower concentrations and shorter exposure durations than micro-particles. This was due to greater ability of cells to internalize nano-particles leading to increased toxicity [55]. The US Agency for Toxic Substances and Disease Registry conducted an environmental assessment of Fallon [76] and concluded that the dwellings of afflicted families were outside of the atmospheric exposure radius of a local hard-metal manufacturing facility. There remains a lack of consensus as to the cause of the leukemia outbreak, and key questions persist as to whether airborne particle size, concentration, method of ingestion, duration of exposure, or co-toxicity with other contaminants may be contributing factors. Many researchers have rightly identified the need for further research to assess the validity of these hypotheses [53, 73, 75], and caution must be exercised in data interpretation in light of the potential legal implications [71].

Tungsten mobility has been observed within the human body. In an experimental treatment for breast cancer patients, a W-based shield was used during intraoperative radiotherapy. Subsequently, W was detected in the patients' urine at a mean concentration of 1.76 ppb after at least 20-month post treatment [75]. Two patients in that study who received mastectomies as part of their treatment continued to exhibit elevated urine W (2.29–2.71 ppb) 2 years after treatment, indicating mobility and accumulation of W within the human body. A number of studies have identified bone tissue as a reservoir in which W accumulates [75, 77, 78] and which may lead to elevated blood and urine W concentration after direct exposure has ceased. Kelly et al. [78] indicated that prolonged

endogenous exposure to W after cessation of exposure via drinking water likely occurred as a result of its mobilization from storage in the bone, comparable to the storage and release of lead in the skeletons of mine workers. Similar observations of W mobility were reported by Centeno et al. [79], in which soft tissue surrounding embedded ammunition fragments in U.S. military personnel exhibited elevated W concentrations. It is worth noting, a 2015 report on W toxicology suggested that W species are not bioavailable through dermal exposure and are not acute toxicants, eye and skin irritants, or dermal sensitizers, nor was tungsten determined to be a carcinogenic [80]. The reliability of this conclusion is questionable, however, as several studies have correlated W exposure to carcinogenic effects. Kelly et al. [78] reported dose-dependent DNA damage leading to impaired B cell development in mice subjected to chronic W exposure via drinking water. It is hypothesized that this behavior may directly contribute to leukemogenesis, particularly in utero, when B cells are present in high concentrations, or in early childhood due to extensive bone development and remodeling [78]. In vitro testing of human bronchial cells and in vivo testing using a rat model found anchorage-independent cellular growth and tumorigenesis, respectively, as a result of W exposure, with notable dysfunction of the S100A4 gene, which has been associated with lung cancer in humans [81]. Dismissal of the potential carcinogenic role of W due to relatively limited human studies, as in the 2015 report, may therefore lead to an underestimation of the risk posed by this element. Such assertions must be re-examined in light of the extensive in vitro studies and rat models.

Studies have also determined associations between W and various human diseases in addition to the potential linkage to leukemia. Menke et al. [82] determined associations between urine W and diabetes although not with insulin resistance; Navaz-Acien et al. [83] found significant relationship between urine W and cardiovascular disease; and Christensen [84] observed changes in thyroid function with exposure to W. Rotter et al. [85] examined elevated blood heavy metals and diagnosis of metabolic syndrome (MS) in men aged 50–75. Whereas direct correlation between W and MS was not found, statistically significant positive correlations between W and total cholesterol and low-density lipoproteins, and significant negative correlations with insulin levels were reported. The researchers of that study suggested that W may contribute to lipid disorders. Studies of tungsten's effect on rats produced differing results than the human-based investigations. For example, Barberá et al. [86] reported remediated symptoms including improved cellular function, reduced mortality, and limitation of changes to kidney morphology in diabetic rats treated with tungstate, and Nagareddy et al. [87] reported improved cardiac performance. It therefore, remains unclear as to whether rodents are an appropriate model for W effects on humans, or whether specific W species may be developed into

effective treatments for common human ailments. This was in a study on W effects on rat and human liver cells [44]. Several authors have identified co-occurrence and co-exposure of W with other metals and metalloids [88], particularly arsenic [89, 90], molybdenum and uranium [83], and cobalt [53, 54], some of which are noted for their own toxicity. Lemus and Venezia [80] identified potential human health issues when W is involved with other metals and metalloids such as antimony and cadmium. It is therefore difficult to ascertain whether the observed effects on the human body are directly attributable to W or to other contributing factors [91, 92]. This was the case in a study of lung cancer among workers in a W processing



**Fig. 2** Flowchart indicating the conceptual pathway from environmental source to health effect of W. While most stages of this pathway are confirmed, the mechanisms of biological activity require further elucidation

facility in France [93], who were co-exposed to cobalt, a known carcinogen. Co-occurrence may contribute to altered W toxicity, although mechanisms of interaction are poorly understood. An *in vitro* study of W toxicity to human cells reported LD<sub>50</sub> of 50, 100, and 1000 µg mL<sup>-1</sup> for pulmonary arterial endothelial, smooth muscle, and dermal cells, respectively [94]. These researchers concluded that the low rate of degradation of W coils used in medical implants is unlikely to lead to serum concentrations exceeding these thresholds. However, it has not been determined whether such concentrations may be exceeded as a result of prolonged environmental exposure. Notably, pulmonary cells were shown by this study to be most vulnerable to W toxicity, which concurs with reports of lung cancer in workers exposed to W and other heavy metals [91, 93]. Furthermore, adsorbed or ingested W can cause nephrotoxicity in doses >125 mg kg<sup>-1</sup>day<sup>-1</sup>, similarly to other metals [80].

Whereas a definitive statement on the mechanisms of W toxicity in human beings cannot be made, the frequency and extent of studies reporting correlations between exposure and adverse health is a cause for concern. By comparison, methemoglobinemia is a well-understood illness that may occur as a result of environmental exposure to elevated NO<sub>3</sub><sup>-</sup>-N in drinking waters. We draw this comparison with nitrate levels in drinking waters since it is an established toxicant in the environment at certain high levels [95]. The mechanisms of NO<sub>3</sub><sup>-</sup>-N toxicity within the body are understood, and so the chain of evidence, from source to effect, is established. Conversely, although sources, pathways of ingestion, and clinical manifestations associated with W have been confirmed in the literature, limited consensus has been reached regarding the causes of these symptoms (Fig. 2). Review of studies on W toxicity does, however, reveal an almost ubiquitous call for further research on this crucial knowledge gap [28, 56, 57].

## Conclusions

The burgeoning literature concerning W ubiquity and toxicity suggests that, contrary to previous assumptions, it potentially represents a significant threat to both human and environmental health. It is therefore rightly classed as an emerging contaminant, which merits further research over the coming years in order to fill the present knowledge gaps. What are the mechanisms by which W affects biotic health? How can these health effects be remedied? What are the safe thresholds for environmental concentrations? Can remediation techniques be developed for contaminated environments? Are there safer mining and production techniques which may be employed? Are there any threats resulting from incidental exposure through W products? These are only a few of the many important questions which must be investigated in order to understand and successfully utilize this global commodity.

Critically, consensus must be reached regarding the mechanisms of W activity within the human body, and consequences for human health, as effective methods of addressing any health risks posed by this mineral, are a matter of urgency.

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## Compliance with Ethical Standards

**Conflict of Interest** On behalf of all authors, the corresponding author states that there is no conflict of interest.

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