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Metal ecotoxicity in sea anemones: Accumulation, effects, and knowledge gaps

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ABSTRACT

Metals are a major class of legacy pollutants that end up in marine ecosystems, posing a significant threat to marine biota, including sea anemones. The current review critically synthesises studies published over the last 50 years on the uptake, tissue distribution, and biological effects of 20 metals across 18 sea anemone species in both field and laboratory settings, including interactions with climate change stressors (salinity and pH). Field studies have focused on bioaccumulation and report the high capacity of sea anemones to accumulate metals, mainly iron and barium, primarily in the pedal disk. Laboratory exposure studies reveal a dose- and time-dependent accumulation and highlight that symbionts take up and store essential metals (Cu, Fe, and Mn) due to their key biological roles. Available data point to *Exaiptasia pallida* as a promising model for metal ecotoxicology. Across studies, metals elicit alterations at molecular to behavioural/morphological levels, including transcriptome reprogramming, oxidative stress, and detoxification failures, as well as genotoxicity, cellular injury, immune dysfunction, metabolic and morphological disruption, reproductive impairment, and bleaching, which are generally amplified by climate change stressors. Ultimately, this review identifies key knowledge gaps and outlines future research directions on metal ecotoxicity in sea anemones. Collectively, these insights position sea anemones as informative sentinels of metal contamination in marine ecosystems.

1. Introduction

The marine environment is facing unprecedented anthropogenic pressure from diverse sources, including overexploitation of natural resources, introduction of invasive alien species, maritime transport, climate change, and pollution (Vargas-Fonseca et al., 2024). Among these pressures, pollution poses a significant challenge, resulting in biodiversity and economic losses, and ultimately affecting human health (Landrigan et al., 2020). Major pollutant classes include plastics, chemicals, petroleum, pesticides and fertilisers, pharmaceuticals, and metals (Landrigan et al., 2020). This review focuses on metals, as they are non-biodegradable, globally distributed, and prone to accumulate in hotspots, which further impacts local biota.

Metals and metalloids, hereafter referred to as “metals”, are defined as naturally occurring elements that have a high atomic weight and a density at least five times greater than that of water (Tchounwou et al., 2012). Metals are ubiquitous at low concentrations in most marine environments due to their natural occurrence in crustal rock, sediments, atmospheric deposition, hydrothermal vents, and riverine inputs (Morel and Price, 2003). Metals can also reach marine ecosystems due to anthropogenic pressures via mining processes, sewage discharges, industrial effluent treatments, shipping activity, refineries, effluent and run-off from agriculture, metallic bulk waste, fossil fuel combustion, sacrificial anodes on boats, and via leaching from metal-based antifouling paints (CICAD, 2004; Howe et al., 2012; Lozano-Bilbao et al., 2024c). These activities have the potential to locally increase metal concentrations up to a dozen milligrams per litre, depending on the metal type (Pan and Wang, 2012), and further represent a threat to marine ecosystem health.

Some metals are classified as essential (e.g., copper (Cu), iron (Fe), manganese (Mn), selenium (Se), and zinc (Zn)) due to their key role in enzyme cofactors, protein synthesis, and oxygen transport (Osredkar and Sustar, 2011). Other metals are non-essential (e.g., mercury (Hg), cadmium (Cd), silver (Ag), and lead (Pb)) because they have very

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limited biological functions (Jeong et al., 2023; Sousa et al., 2024). Metal exposure, whether essential or non-essential, can cause an array of adverse effects in marine organisms when concentrations fall outside homeostatic ranges (Krishna et al., 2025). Depending on the type of metal ions and the organism's assimilation strategy, metals can enter cells and readily accumulate in organisms such as molluscs, crustaceans, algae, and cnidarians. Moreover, due to biomagnification, some metals (e.g., Hg) increase their concentration progressively along the food chain, reaching high levels in top predators, and having severe negative impacts at the organism, population, and community levels (Clements and Rohr, 2009; Danovaro et al., 2023).

Due to its known toxicity and ecotoxicological effects, metals have been investigated since the early 1960s (Nordberg et al., 2007), using a range of representative taxa, e.g., bivalves, crustaceans, and fish, to evaluate marine environmental health (e.g., NOAA Mussel Watch Program, (Sparks et al., 2014). Nonetheless, many taxa, such as cnidarians, have received minimal attention despite their importance in ecosystems and in providing crucial ecosystems services, such as, habitat provisioning, biotechnological applications, or nutrient cycling. For example, sea anemones play a key role in the food chain, acting as a link between the pelagic and benthic food dynamics, and playing a key biogeochemical role in the benthic ecosystem (Howe et al., 2012; Menezes and Thakur, 2022). Furthermore, relying solely on classical models may not accurately capture the potential impact and responses to metal contamination across diverse biological groups (Gutierrez et al., 2024). For this reason, the use of both classical and understudied models will provide a broader understanding of metal accumulation and its likely consequences for marine ecosystem health, underscoring the interest in cnidarians as biological models for metal accumulation and toxicity.

Cnidaria are an ancient phylum that includes corals, sea anemones, jellyfish, and hydra (Howe et al., 2012). The cnidaria have a worldwide distribution from polar to tropical regions and are found from the deep sea up to intertidal zones (Brock and Bielmyer, 2013; Fautin et al., 2013; Escobar-Chicho et al., 2019). Among cnidarians, sea anemones are sessile anthozoan polyps that feed predominantly on zooplankton and small invertebrates (Howe et al., 2012), with both asexual (through longitudinal/transversal fission or pedal laceration) and sexual reproduction comprising briefly 4 key stages: gametes, planula larvae, settlement and juvenile (metamorphosis), and adult polyp (Fautin, 2002; Brandão et al., 2025). Sea anemones can exist with photosynthetic dinoflagellates (symbiotic) or without them (aposymbiotic). These dinoflagellates, known as zooxanthellae from the family *Symbiodiniaceae* (formerly referred to as genus *Symbiodinium*) (LaJeunesse, 2020), supply the host with energy, translocating their fixed carbon to the host, covering much of the host's energetic demand and supporting growth and reproduction (Davy et al., 2012). Symbionts also reshape host metabolism and stress physiology, including respiration rates, nitrogen cycling, and redox balance (e.g. baseline reactive oxygen species (ROS) production and antioxidant capacity) (Downs et al., 2002; Yellowlees et al., 2008; Nitschke et al., 2022). At the same time, the sea anemone offers protection and resources in return (Goulet et al., 2005).

Sea anemones have been highlighted as candidate model organisms for ecotoxicological studies since they are easy to collect and maintain in captivity, have low mobility, are sensitive to a wide range of contaminants, and can accumulate metals in their tissues, leading to measurable biological effects (Howe et al., 2012, 2014a; Anjos et al., 2014). The effects of xenobiotics (e.g., metals) on organisms are commonly assessed using biomarkers. These are functional indicators of stress that can be measured at the sub-organismal, physiological, or behavioural level (Galloway, 2006). However, the impact of metals and their complex mixtures on sea anemones remains poorly understood and requires further study.

Alongside pollution, sea anemones face additional stressors that are associated with accelerating climate change (Ringwood et al., 2025). Variations in water temperature, salinity, and pH can modify metal speciation and partitioning, increasing their bioavailability and, consequently, their toxicity, strengthening their negative impacts on animal biology and survival (Horwitz et al., 2014; Siddiqui and Bielmyer-Fraser, 2015; Trenfield et al., 2017; Anjos et al., 2019). It is also well documented that changes in temperature or pH can cause bleaching, a process involving the loss of symbionts (e.g., *Breviolum muscatinei*, and *Elliptochloris marina*) and their photosynthetic pigments in sea anemones (Hill and Scott, 2012; Hoepner et al., 2019; Carrier et al., 2025).

To date, research on metal uptake, storage, and excretion has elucidated the key role of symbionts in metal regulation in sea anemones (Mitchelmore et al., 2003a, 2003b). Although aposymbiotic sea anemones can accumulate higher levels of some metals (e.g., Cu) than their symbiotic counterparts (Harland and Nganro, 1990; Main et al., 2010). This suggests that the pathways involved in metal uptake/accumulation are not fully understood, particularly because they are specific to each metal and differ between symbionts and aposymbionts. Moreover, research on the effects of metals on sea anemones is limited, with most studies focusing on behavioural responses (e.g., tentacle retraction) as potential biomarkers of metal exposure (Ianna et al., 2020). Whilst the effects at biochemical (e.g., metallothionein, oxidative stress, neurotoxicity, and genotoxicity markers) and molecular level (transcriptomics, proteomics, metabolomics) are poorly studied, the development of early-warning biomarkers in this taxa is essential for evidence-based environmental management, including biomonitoring programs and environmental risk assessment.

This review provides a critical synthesis of studies on metal accumulation in sea anemones, covering the period from 1977 to 2025, encompassing both field and laboratory experiments. It examines the accumulation patterns and biological effects of specific metals, including aluminium (Al), antimony (Sb), arsenic (As), barium (Ba), cadmium (Cd), chromium (Cr), cobalt (Co), copper (Cu), iron (Fe), mercury (Hg), lithium (Li), manganese (Mn), nickel (Ni), lead (Pb), selenium (Se), silver (Ag), Strontium (Sr), Titanium (Ti), Vanadium (V), zinc (Zn). Additionally, it examines the impact of climate change stressors on metal accumulation and toxicity in sea anemones at the molecular, biochemical, and cellular levels. Key knowledge gaps are identified, and future needs for research on metal ecotoxicity in sea anemones are identified.

2. Materials and methods

2.1. Search strategy and criteria

The mnemonic tool Population, Intervention, Comparison, and Outcome (PICO) was used to elaborate the research questions and the search strategy (Table S1) (Fineout-Overholt and Johnston, 2005). The search strategy was conducted in two different databases for this review: Web of Science (WoS) and Scopus, with the literature search undertaken between March and April 2025. Searches only considered English-published studies, and the keywords used were “sea anemone” AND “ecotoxicology” OR “heavy metal” OR “metal*” OR “biomarker” OR “metal exposure” OR “metal accumulation” OR “accumulation” OR “molecular biomarker” OR “bioaccumulation” OR “omic” OR “transcriptomic” OR “proteomic” OR “metabolomic” OR “transcriptome” OR “proteome” OR “metabolome” OR “climate change” OR “combined effects” OR “multiple stressors”. The plurals of these keywords were also used.

For the inclusion and exclusion criteria, we considered only primary peer-reviewed research articles, regardless of their publication date, while excluding grey literature. Excluded sources comprised non-English publications, presentations, books or chapters, reviews, reports, comments, monographs, academic theses, and studies outside the scope of this review. Reviews were excluded to avoid data duplication; however, their reference lists were cross-checked against our reference database to ensure that no relevant primary literature were overlooked.

2.2. Selection, categorization, and analysis of publications

The publication selection process followed a three-tier approach consisting of identification, screening, and inclusion, as outlined in the PRISMA 2020 framework (Page et al., 2021). The screening process included two steps: in the first step, we assessed the titles and abstracts of each study, and in the second step, we reviewed the full texts of the selected studies.

Searches were conducted between March and April 2025, and 1158 studies were retrieved, 601 from the Web of Science (WoS), 547 from Scopus, and 10 cross-referenced studies. All records were imported into Mendeley Desktop (version 2.130.2), and duplicate documents were removed ($n = 380$). Following this, 778 studies were screened by title and abstract, resulting in the exclusion of 697 studies due to non-compliance with at least one of the search criteria. The full texts of 86 articles were assessed for eligibility. Only those records that satisfied every criterion were included. Ultimately, 48 studies met all inclusion criteria, while 46 records were excluded due to unsuitable outcomes or publication types (Fig. S1).

Extracted data included publication year, country of the corresponding author, sea anemone species, metals used for exposure or analysed, sampling location, and exposure setting (in situ or ex situ). For experiments, the following details were recorded when applicable: metal type, exposure duration and concentration, exposure method (in vitro, using anemone cells; in vivo, using the whole live organism; or ex vivo, using slices of organ tissue), methodological approach (metal accumulation, endpoint biomarkers, gene expression, transcriptomics, proteomics, behavioural assays), and tissue analysed.

3. Results and discussion

3.1. Historical overview and geographic distribution

A total of 48 papers were considered for this review, covering studies on metal accumulation and/or effects in sea anemones published between 1977 and 2025 (Fig. 1A). Research, from 1977 to 2013, was low intensity, with an average of less than one article per year (~0.44). The first article screened was published by Evans (1977) and evaluated the long-term toxicity of Cu on the mortality of *Aiptasia diaphana*, highlighting the potential of sea anemones as models for metal accumulation (Evans, 1977). In 1990, Harland and Nganro reported the first behavioural effects of Cu exposure in *Anemonia viridis*. In the 2000s, articles reported studies with the metals Cu, Cd, Hg, Zn, Ni, and Pb and incorporated biochemical and molecular endpoints (Gilbert and Guzmán, 2001; Mitchelmore et al., 2002, 2003a). From 2013 to date, there has been a relatively rapid increase in articles (averaging ~3.1 per year), and the use of advanced techniques (e.g., Anjos et al., 2014; Elran et al., 2014). Notably, the first RNA-seq analysis of *Nematostella vectensis* exposed to Cd, Cu, Hg, and Zn occurred in 2014 (Elran et al., 2014). Whereas Anjos et al. (2014) assessed Cu effects on isolated and cultured cells from lacerates of the pedal disc of *Bunodosoma cangicum*. During the last decade, the use of sea anemones as bioindicator models for field-based metal pollution studies worldwide has been consolidated (e.g., Horwitz et al., 2014; Ansari et al., 2016; Escobar-Chicho et al., 2019; Lozano-Bilbao et al., 2020). Furthermore, articles came from across the globe and the 12 countries that published at least one paper per year includes the United States, Australia, Spain, Brazil, Italy, Japan, the United Kingdom, Israel, Lebanon, France, Mexico, and Russia (Fig. 1B). Four countries: the United States, Australia, Spain, and Brazil, accounted for 75% of the articles published. Italy contributed ~6%, while Japan, the United Kingdom, and Israel each contributed ~4%, and Lebanon, France, Mexico, and Russia contributed ~2% each (Fig. 1C).

3.2. Metal accumulation on sea anemones

Metals, whether essential or non-essential, can accumulate in sea anemones through multiple routes, depending on the metal type, assimilation efficiency, and route of exposure (Brock and Bielmyer, 2013; Anjos et al., 2019; Trenfield et al., 2017). Uptake can occur mainly via direct contact with water, sediment or substrates, or ingestion of contaminated particles (Horwitz et al., 2014; Lozano-Bilbao et al., 2024c). In addition, sea anemones, like other cnidarians, can accumulate metals through their symbiotic association with zooxanthellae. These symbionts are located within the host's gastrodermis, with the highest densities in the tentacles and, to a lesser extent, in the oral disc, column, and pedal disc (Dimond et al., 2013; Tivey et al., 2022). Besides supplying photosynthetically derived energy, zooxanthellae can enhance metal uptake via membrane-bound metal transport systems, allowing the assimilation of dissolved and free ions and small metal-conjugated complexes from both host fluids and the surrounding water (Monteiro et al., 2012; Rodriguez and Ho, 2018). Due to their high abundance, elevated metabolic activity, and requirement for essential metals (e.g., Fe, Mn, Cu, and Zn), symbionts also contribute to metal accumulation and storage, acting as a sink for metals within host tissues (Mitchelmore et al., 2003b; Davy et al., 2012; Howe et al., 2014a). In contrast, the role of symbionts in the uptake and accumulation of non-essential metals, as well as the extent of partitioning between zooxanthellae and host tissues, remains poorly understood. In addition, symbionts increase endogenous ROS production during photosynthesis, resulting in tissue hyperoxia, which stimulates host antioxidant defences. This includes an increase in basal antioxidant defence diversity (i.e., isoforms) and activity (Richier et al., 2005). Moreover, symbionts also promote antioxidant reorganisation within host tissues, leading to higher expression and activity of antioxidant enzymes in symbiont-containing regions (e.g., gastrodermis) compared with a more homogeneous distribution across host tissues (Hawkridge et al., 2000; Pey et al., 2017), thereby increasing host redox capacity. This section critically reviews field and laboratory data on metal accumulation in sea anemones and presents mechanisms of metal uptake, storage, and regulation.

As summarized in Tables S2 and S3, field studies have measured a wider range of metals (20 in total: Ag, Al, As, Ba, Cd, Cr, Co, Cu, Fe, Hg, Li, Mn, Ni, Pb, Sb, Se, Sr, Ti, V, and Zn) compared to laboratory exposure experiments, which have focused on six metals (Cd, Cu, Hg, Mn, Ni, and Zn). However, in field studies, some metals were reported only once: Sb, Se, and Ti in the sea anemone *P. pabista* collected at the hydrothermal system of Guaymas Basin, United States of America (Escobar-Chicho et al., 2019), and Hg in *B. caissarum* from Guanabara Bay, Brazil (Ansari et al., 2016). Further, in laboratory-based studies Hg accumulation in *Actinia equina* was reported once (Gadelha et al., 2010). Regarding the tissues analysed for metal accumulation, whole-anemone was the most commonly studied (60%), followed by the pedal disc (11.4%), tentacles (8.5%), muscle (8.5%), oral disc (2.8%), and cell cultures from pedal disc (2.8%).

3.2.1. Metal accumulation on field-collected sea anemones

Metal accumulation in field-collected sea anemones varied significantly across geographical, physiological, and methodological factors. Geographical differences include levels and sources of contamination, as well as exposure to multi-metal realms. Physiological drivers, such as species-specific traits, also influence metal uptake and storage. Methodological variability further contributes to discrepancies among studies, as different measurement techniques, such as Inductively Coupled Plasma Mass Spectrometry (ICP-MS), which offer high sensitivity, or Atomic Absorption Spectroscopy (AAS) and ICP - Atomic Emission Spectroscopy (ICP-AES), which are more cost-effective and suitable for multi-element analysis, may differ in sensitivity due to quantification capability (e.g., detection limits, precision, or matrix effects). Still, when properly calibrated and subjected to appropriate quality control, these methods generally produce comparable results. Additionally, expressing metal concentrations on either a dry weight (dw) or a wet weight (ww) basis introduces further inconsistency.

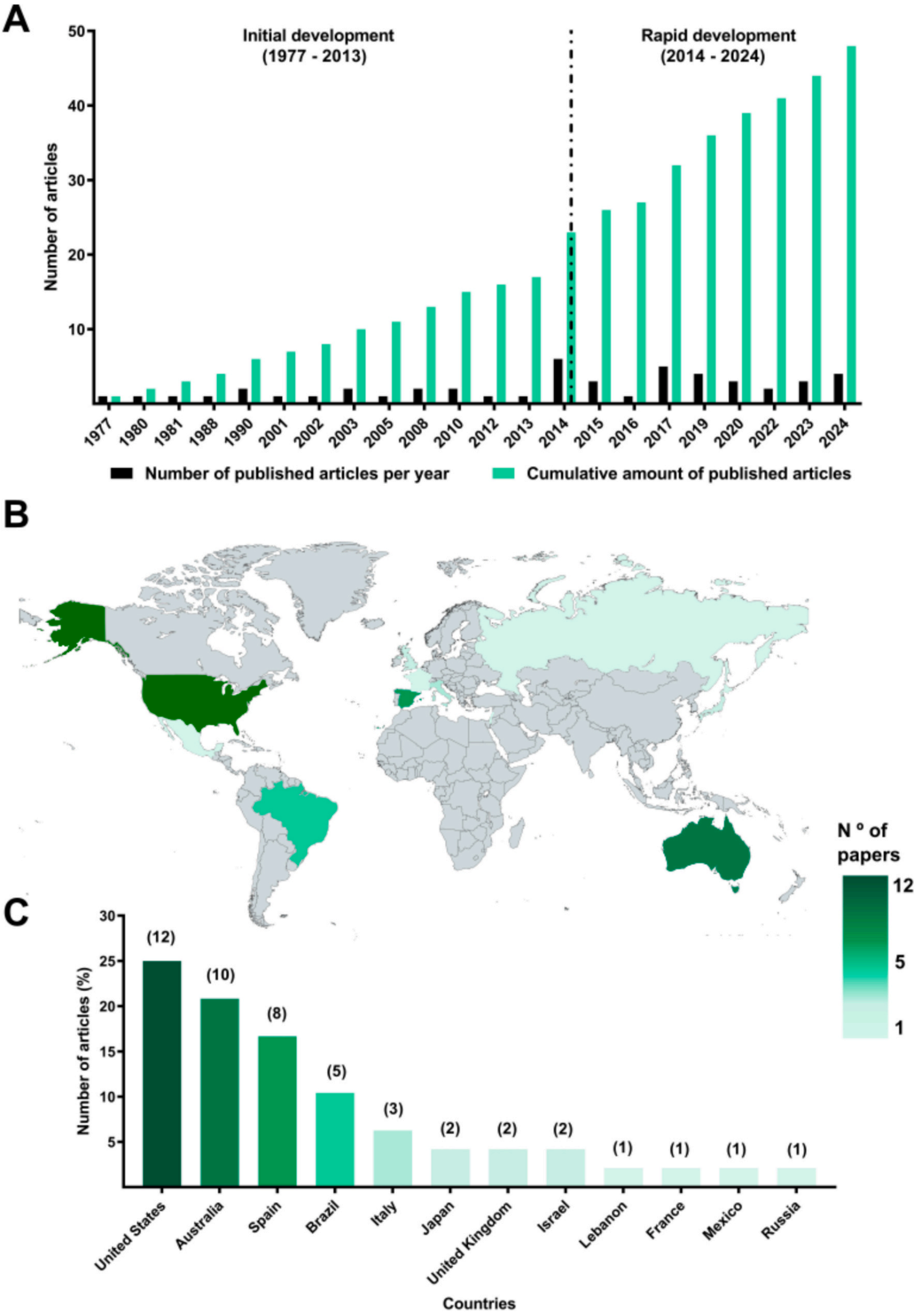

Fig. 1. (A) Annual publications (black) and cumulative total (green) on metal accumulation and effects in sea anemones. (B) Global geographic distribution of studies. (C) Per-country article counts are shown as a bar chart, with countries shaded in green tones according to the number of articles published. The number of articles is indicated in brackets above the green shaded bar chart in panel C. The figure was created using GraphPad Prism (version 9.0) and Inkscape (version 1.4). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Together, these confounding factors complicate direct comparisons across studies. Nevertheless, a general trend among studies is an increasing metal body burden, in the following sequence: Fe > Ba > Al > Zn > Sr > Mn > Cu > As > Pb > Hg > Ni > Cr > Ti > Se > V > Li > Sb > Cd > Co (Table S2). In the following results and discussion, the metals are presented in the same sequence, and a summary is provided in Fig. 2.

Fe accumulation occurs across all sea anemone tissues (Horwitz et al., 2014; Corrias et al., 2020; Lozano-Bilbao et al., 2020) and reaches the highest concentrations of all metals analysed to date, with up to 24,300 μg/g dw in *Actiniaria* spp. from the Broken Spur hydrothermal field, in the Mid-Atlantic Ridge (Demina and Galkin, 2008). Tissue-specific partitioning shows preferential Fe storage in the pedal disc of *Anemonia viridis,* potentially due to direct contact with the metal-rich sediment (Horwitz et al., 2014). In tentacles, up to 85% of Fe is found in the algae symbiotic fraction rather than in the sea anemone's tissue (Horwitz et al., 2014), probably due to the key role of this metal in symbiont growth and photosynthesis (Reich et al., 2020).

Ba reaches tissue concentrations of up to 14,247 μg/g dw in *Paraphelliactis pabista* from the hydrothermal system of the Guaymas Basin (Escobar-Chicho et al., 2019). In both *A. viridis* and *P. pabista*, the pedal disc is the primary target organ for Ba accumulation (Horwitz et al., 2014; Escobar-Chicho et al., 2019), possibly due to its direct contact with Ba-rich sediments (Horwitz et al., 2014), thereby favouring its assimilation.

Al levels varied from 1.41 ± 0.37 to 25.33 ± 2.47 μg/g ww in *Anemonia sulcata* collected from unpolluted and polluted sites, respectively, along the Canary Islands (Lozano-Bilbao et al., 2024a, 2024b). Across the tissues analysed, Al accumulated in the pedal disc compared to the oral disc, muscle, tentacles, or whole-anemone samples (Escobar-Chicho et al., 2019; Corrias et al., 2020; Lozano-Bilbao et al., 2024c).

Zn is the most frequently analysed metal and was measured in over 70% of the field studies considered (Table S2). Zn distribution in sea anemone tissues was relatively uniform, including whole animal extracts, muscle, oral disc, and column, likely reflecting its essential role in diverse biological processes (Table S2). Nevertheless, Zn accumulation in the pedal disc of *A. viridis* was higher than in tentacles (Horwitz et al., 2014), which, taken together with the data for Al, Fe, and Ba, suggests that the pedal disc may serve as a storage site. In addition, the pedal disk offers significant information from a biomonitoring perspective. It provides a sensitive and pathway-specific measure of sediment- and substrate-associated metal exposure compared to tentacles or whole-organism homogenates. Due to its direct and prolonged contact with sediments and rigid substrates, metals bound to these matrices can accumulate locally to much higher concentrations than in tissues primarily exposed via the water column. In contrast, whole-organism homogenates integrate multiple tissues with different exposure routes and provide an overview of accumulation, although they may dilute metal concentrations, further hindering localised storage.

Sr similarly accumulates preferentially in the pedal disc rather than other body locations (e.g., tentacles and column) of *A. viridis* and *P. pabista* (Escobar-Chicho et al., 2019; Corrias et al., 2020), potentially due to its local accumulation through direct absorption from Sr-rich sediments.

Mn had low accumulation in tentacles (0.22–0.35 μg/g ww) of *A. sulcata* from polluted (industrial effluents) and clean sites at Sardinia Coast (Corrias et al., 2020), whereas the pedal discs of *A. viridis*

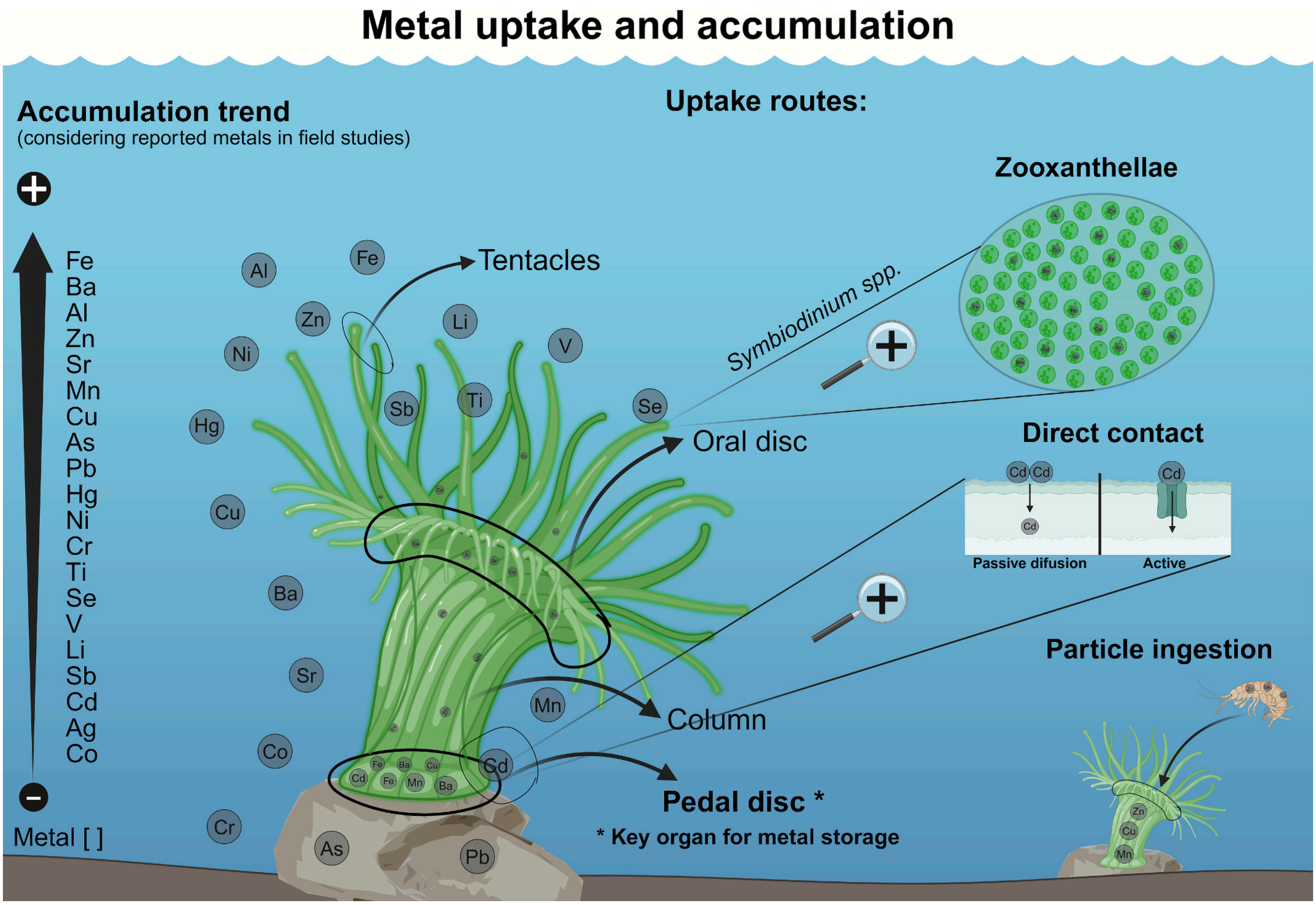

Fig. 2. Trend of metal accumulation and the role of tissue in metal accumulation, storage, and partitioning of field-sampled sea anemones. This figure was created with BioRender.com.

accumulated more Mn (3.5 ± 0.14–15 ± 3.20 μg/g dw) from a CO_2 vent site at Levante Bay (Horwitz et al., 2014). This low Mn accumulation in tentacles could be due to Mn sources, as Mn inputs in seawater are often associated with riverine and continental inputs, as well as atmospheric deposition (Morel and Price, 2003), leading to deposition in sediments where anemones can interact through their pedal discs, potentially facilitating absorption and accumulation. In contrast, sea anemones from hydrothermal systems are shown to accumulate Mn in the column preferentially (194 ± 1.58 μg/g dw) (Escobar-Chicho et al., 2019). This accumulation preference may be attributed to the filter-feeding habits of *P. pabista*, in which Mn body burden enrichment occurs through feeding, a feeding behaviour known to be Mn-enriched in hydrothermal systems (Escobar-Chicho et al., 2019).

Cu accumulation ranges from 0.16 μg/g ww in tentacles of *A. sulcata* collected along the Sardinia Coast (Corrias et al., 2020) to 1165.40 μg/g dw in the whole tissue of *Actiniaria* spp. from the Mid-Atlantic Ridge (Demina and Galkin, 2008). Regarding Cu partitioning among tissues, the pedal disc appears to accumulate higher Cu levels than the tentacles in *A. viridis* (Horwitz et al., 2014). However, higher Cu accumulation was observed in the symbiotic fraction in the tentacles (Horwitz et al., 2014), which explains the lower Cu levels, as the Cu could be allocated to the symbiont cells.

As accumulation is higher in *Entacmaea actinostoloides,* showing a 2-fold higher body burden than *A. equina* (Ninh et al., 2008). This difference may be partly explained by As speciation in both species, the tetramethylarsonium ion (TEMA) was the dominant form, whereas *A. equina* lacked arsenobetaine (AB) (Ninh et al., 2008), the primary As compound typically found in marine organisms (Shiomi, 1994). The absence of AB could account for the lower total As levels in *A. equina*. These studies highlight that metal chemistry, rather than total concentration alone, can govern both the extent of accumulation and potential toxicity, as different chemical forms vary in bioavailability, uptake routes, and detoxification mechanisms. This has been demonstrated in the cnidarian model *Millepora alcicornis,* where free ionic and certain organometallic species were more bioavailable and toxic than strongly complexed forms (de Freitas Neto et al., 2025). However, species identity is not the sole determinant; environmental conditions such as location and bioavailability also influence accumulation. For example, *A. equina* collected along the Chiba coast accumulated three times more As than individuals from Tokyo Bay (Shiomi et al., 1988; Ninh et al., 2008).

Regarding **Pb** accumulation, *A. sulcata* from the Canary Islands shows no clear difference between whole tissue and muscle regardless of the contamination site status (Lozano-Bilbao et al., 2020, 2023a, 2023b, 2024a, 2024b, 2024c). Nonetheless, *A. sulcata* is an efficient Pb accumulator, exhibiting up to 190-fold (0.13 ± 0.15–25.26 ± 47.18 μg/g ww) whole-tissue enrichment between unpolluted and polluted sites (Lozano-Bilbao et al., 2020), suggesting strong potential as a Pb bioindicator. In contrast, studies that examined multiple tissues (pedal discs, oral discs, and column) revealed preferential Pb accumulation in the pedal disc in *P. pabista* with an accumulation up to 44.08 μg/g dw, 3-fold higher than in the oral disc or column (15.65 ± 0.63 and 10.66 ± 0.59 μg/g dw, respectively) (Escobar-Chicho et al., 2019). While in *A. viridis*, concentrations were up to 75-fold higher in the pedal disc compared to tentacles (Horwitz et al., 2014). These findings suggest that the pedal disc is a primary site of Pb accumulation in *A. viridis* and *P. pabista*. Whether the same pattern occurs in *A. sulcata* remains unclear, as pedal disc tissues were not analysed in the available studies.

A. sulcata has proven to be a reliable bioindicator of **Ni** accumulation, reflecting significantly higher concentrations at polluted sites (2.18 ± 3.07 μg/g ww) (high anthropogenic activities and high influx of Saharan dust) than at unpolluted ones (0.09 ± 0.05 μg/g ww) in the Canary Islands (Lozano-Bilbao et al., 2020, 2024b). In terms of tissue partitioning, no clear preference was reported in either *A. sulcata* or *P. pabista* (Escobar-Chicho et al., 2019; Lozano-Bilbao et al., 2020). Conversely, *A. viridis* from Vulcano Island showed markedly higher Ni levels in the pedal disc than in the tentacles (0.35 ± 0.03 and 0.075 ± 0.007 μg/g dw, respectively) (Horwitz et al., 2014), suggesting possible species-specific partitioning. Alternatively, this difference may reflect environmental factors such as Ni source, bioavailability, or route of exposure.

Cr accumulation appears to be tissue-specific, with higher concentrations in pedal discs than in oral discs or tentacles of *P. pabista* and *A. viridis* (Horwitz et al., 2014; Escobar-Chicho et al., 2019). However, the apparent affinity for pedal disc accumulation may reflect Cr availability, exposure route, and exposure duration, which strongly influence body burdens. For instance, *A. equina* collected from polluted locations (e.g., garbage dumping, untreated sewage inflow, land and river runoff, and heavy traffic) along the Ras Beirut coast showed the highest Cr concentrations (11.8 μg/g dw) reported in sea anemones, underscoring the importance of environmental conditions (Shiber, 1981).

Regarding **V**, *A. sulcata* demonstrated substantial bioaccumulation capacity, with up to a 10-fold increase in individuals from highly polluted compared to less impacted sites (Lozano-Bilbao et al., 2020). Likewise, **Li** accumulation has so far only been reported in *A. sulcata* from the Canary Islands, suggesting both species- and site-specific patterns (Lozano-Bilbao et al., 2020, 2024a, 2024b). Moreover, unusually high Li concentrations were detected in anemones from upwelling event zones (Lozano-Bilbao et al., 2024b), likely linked to metal (e.g., Ni) resuspension processes that enhance Ni bioavailability in the water column, promoting its uptake.

Cd is readily accumulated by *A. sulcata*, with individuals from highly impacted harbour areas containing up to 5-fold higher Cd levels (0.010 ± 0.00 μg/g ww) than those from control sites (0.002 ± 0.00 μg/g ww) (Lozano-Bilbao et al., 2023a). Such elevated concentrations may be due to anthropogenic activities common in port environments, including ship maintenance (e.g., antifouling paints), intensive maritime traffic, and fossil fuel combustion, all of which contribute to Cd inputs (Lozano-Bilbao et al., 2023a). Interestingly, *A. sulcata* also appears capable of regulating Cd body burdens in response to changing environmental conditions, during the COVID-19 lockdown, when tourism and coastal anthropogenic pressure in the Tenerife Islands sharply decreased, from 0.004 to 0.001 μg/g ww, Cd concentrations in *A. sulcata* declined, consistent with reduced releases and bioavailability (Lozano-Bilbao et al., 2023b). Regarding tissue-specific accumulation, no significant differences in Cd accumulation have been reported between tissues in either *A. viridis* or *A. sulcata* (Horwitz et al., 2014; Lozano-Bilbao et al., 2023b, 2024a).

Although **Co** exhibited the lowest concentration among the 20 metals analysed, this potentially indicates a generally low affinity for accumulation in sea anemones. However, *A. sulcata* collected from sites with elevated Co availability in the Canary Islands was able to accumulate Co, reflecting the environmental conditions (Lozano-Bilbao et al., 2024b). At the tissue level, *A. viridis* displayed higher Co concentrations in pedal discs (0.34 ± 0.04 μg/g dw) than in tentacles (0.03 ± 0.00 μg/g dw) (Horwitz et al., 2014). In contrast, in *P. pabista,* the opposite pattern was observed, with lower pedal disc accumulation (0.13 μg/g dw) compared to oral discs and the column (0.28 ± 0.08 and 0.31 ± 0.07 μg/g dw, respectively) (Escobar-Chicho et al., 2019). These contrasting findings suggest potential tissue-specific accumulation, however, the underlying mechanisms remain unclear and require further investigation.

Hg, **Sb**, **Se**, and **Ti** concentrations have been reported in only a single study each, limiting comparative analysis. Hg concentrations reached 23.19 ± 3.28 μg/kg ww in *B. caissarum* from Guanabara Bay, near a former Chlor-Alkali Plant that employed Hg amalgam technology for decades (Ansari et al., 2016). Sb, Se, and Ti were detected in *P. pabista* from the Guaymas Basin hydrothermal system, with no significant differences found among tissues (oral, pedal disc, and column) (Escobar-Chicho et al., 2019).

Overall, available field studies demonstrate that sea anemones can accumulate a broad variety of metals reflecting the metal contamination patterns across diverse environments worldwide, which are subject to varying degrees of anthropogenic activity. Metals have been detected in all body compartments, with the pedal disc emerging as the primary site of assimilation and storage for most metals. However, for some metals, including Cu, As, Cd, Pb, and Zn, the primary tissues involved in assimilation and storage remains unclear, owing to the limited number of studies assessing tissue-specific metal accumulation, non-standardised sampling practices across studies, and likely interspecific variability in metal accumulation in the different tissues. When data on tentacles are available, they generally exhibit lower metal concentrations than other tissues (e.g., pedal, oral disc, and whole tissue), possibly due to the presence of zooxanthellae, which can sequester metals within symbiont cells (Iyagbaye et al., 2022a) and thereby reduce concentrations in tentacle host cells. The role of symbionts in metal regulation is poorly characterised in field studies, which tend to emphasise biomonitoring applications rather than mechanistic understanding. This knowledge gap underscores the importance of controlled laboratory studies, which enable the systematic evaluation of key drivers of metal accumulation, including exposure conditions (single vs. mixed metals), temperature, symbiotic status, and interspecific differences. These aspects will be addressed in the following discussion.

3.2.2. *Metal accumulation and effects on laboratory-exposed sea anemones*

Under controlled laboratory conditions, we identified 17 studies that quantified metal accumulation and 39 studies that examined metal-induced effects across 12 different sea anemone species (Table S3). Cu, Cd, Zn, and Ni were the most frequently studied metals, with 19, 10, 8, and 8 studies, respectively, whereas only two studies assessed accumulation under mixed-metal exposures (Table S3). *Exaiptasia pallida (sin. Aiptasia pallida)* was the most used species in laboratory-based trials, appearing in 12 studies and serving as the primary model and bioindicator for evaluating both metal accumulation and associated effects. In the following subsections, laboratory-based metal accumulation and individual effects are discussed. However, integrated discussions are limited by differences in experimental designs (e.g., densities, numbers of specimens, biotic factors (size and life-stage), and abiotic factors (pH, temperature, and salinity) that directly impact the generated outcomes. Nevertheless, for most of the metals examined (Cu, Cd, Zn, Ni, and Mn), clear dose- and time-dependent patterns of accumulation and biological effects were observed. Early life stages (lacerates and juveniles) were generally more sensitive than adults, with sublethal effects occurring at concentrations lower than those causing mortality. Common metal-induced responses included behavioural changes such as tentacle retraction and swelling, as well as bleaching in symbiotic species. A summary overview of metal-induced effects is presented in Fig. 3, and the discussion with metals is addressed in order of frequency with which they were most studied, beginning with Cu, Cd, Zn, and Ni, followed by the less frequently examined metals and their mixtures.

3.2.3. *Cu*

Cu is an essential trace metal with key biological roles, acting as a cofactor in numerous enzymes (Wang et al., 2025). In sea anemones, the balance between physiological requirement and toxicity is tightly regulated and strongly influenced by species identity, symbiotic status, and environmental context. Across taxa, Cu accumulation occurs at relatively low exposure concentrations (10 μg/L) in *A. viridis, Anthopleura elegantissima,* and *E. pallida* (Mitchelmore et al., 2003b; Main et al., 2010), yet the mechanisms governing uptake, partitioning, and detoxification differ markedly. Symbiosis emerges as a key factor shaping Cu handling, although its effects are not uniform. In *E. pallida*, aposymbiotic individuals accumulate higher Cu body burdens than symbiotic conspecifics (Main et al., 2010), suggesting that symbiosis

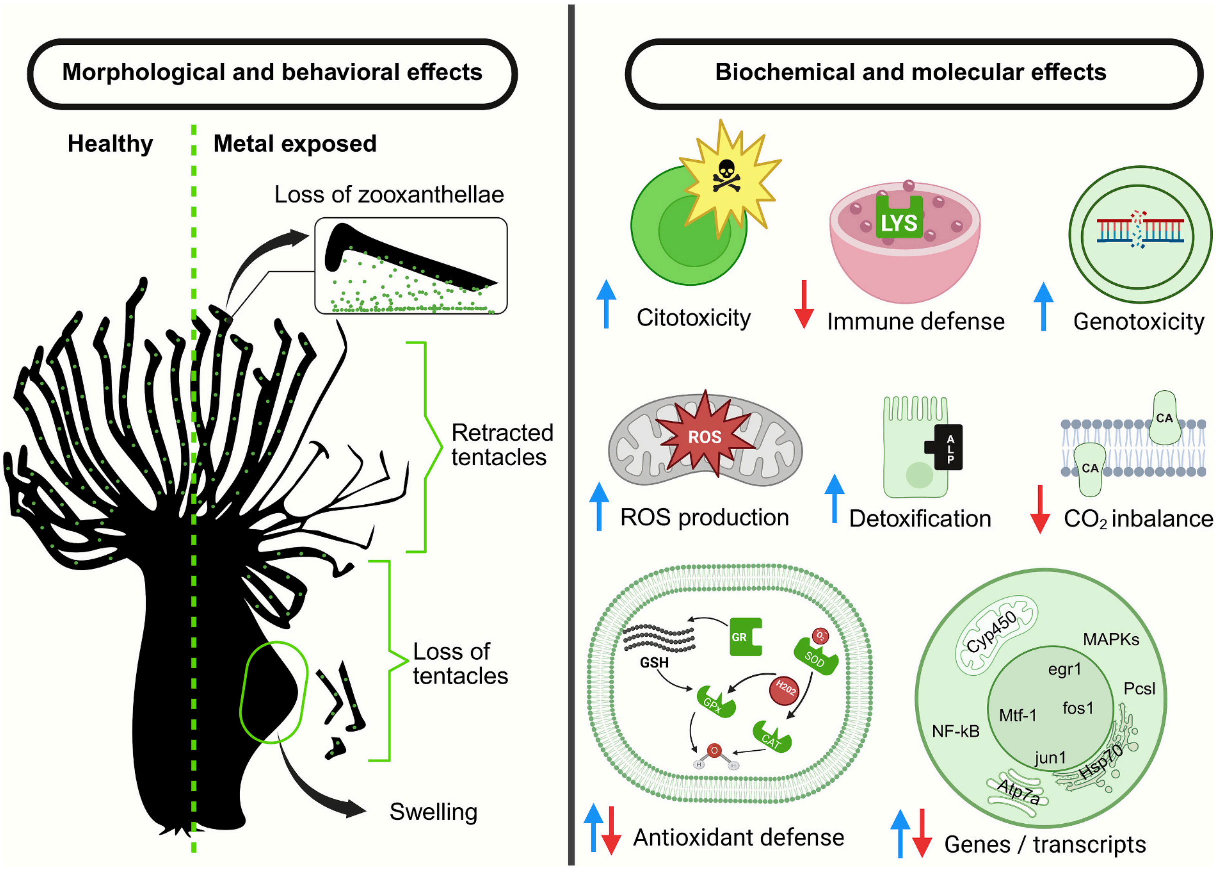

Fig. 3. Main reported biological consequences from a whole animal and molecular perspective of metal toxicity in sea anemones. This figure was created with BioRender.com.

facilitates regulatory processes rather than simple accumulation. Proposed mechanisms include the expelling of zooxanthellae (bleaching) and enhanced mucus production, both of which may contribute to reducing internal Cu loads (e.g., Harland and Nganro, 1990; Main et al., 2010). However, whether bleaching represents an active metal regulatory strategy or a more generalised stress response remains unclear, as bleaching is elicited by a wide range of environmental stressors (Matthews et al., 2016; Cleves et al., 2020). These findings indicate that symbiosis primarily modifies intracellular partitioning and downstream toxicological consequences, rather than acting as a consistent driver of increased metal accumulation. Species-specific differences further modulate Cu tolerance and recovery. *A. elegantissima* can regulate and excrete Cu at concentrations up to 100 μg/L. (Mitchelmore et al., 2003b), albeit requiring prolonged recovery periods (up to 42 d) (Mitchelmore et al., 2003b), indicating effective but slow detoxification pathways. In contrast, *E. pallida* shows limited short-term recovery (7 d), following comparable exposures, with a long-term recovery remaining scarce (Brock and Bielmyer, 2013).

Beyond biological traits, abiotic factors strongly influence Cu availability and toxicity. Reduced salinity and pH conditions, relevant under climate change scenarios, enhance Cu uptake and accumulation in *E. pallida* by increasing metal bioavailability (Millero et al., 2009; Patel and Bielmyer-Fraser, 2015). The chemical form of Cu also plays a critical role, with soluble Cu chloride ($CuCl_2$) being assimilated more rapidly than Cu oxide nanoparticles (CuO NPs) due to faster ion release (Cu^{2+} ions). However, particle uptake pathways may still contribute to nanoparticle assimilation (Siddiqui et al., 2015).

Cu induces both lethal and sublethal effects across sea anemones species, with sensitivity varying according to symbiotic state, life stage, and temperature. Symbiotic *E. pallida* are more sensitive than aposymbiotic individuals (96 h 50% lethal concentration (96 h-LC_{50}): 148 vs 206 μg/L, respectively), likely due to increased Cu sequestration by zooxanthellae and subsequent ROS generation (Main et al., 2010). Elevated temperatures further exacerbate Cu toxicity, amplifying oxidative stress responses (Trenfield et al., 2017; Ianna et al., 2020). Comparatively, *Aiptasia pulchella* exhibits high sensitivity to both acute and chronic Cu exposure, particularly during early life stages, supporting its suitability as a model species for toxicity testing (Main et al., 2010; Howe et al., 2012; Howe et al., 2014c).

At cellular, biochemical, and molecular levels, Cu exposure triggers stress responses, including cytotoxicity, genotoxicity, altered metabolism, antioxidant activity, and oxidative stress. Antioxidant enzymes, including catalase (CAT), glutathione peroxidase (GPx), and superoxide dismutase (SOD), are rapidly mobilised, with symbiotic *E. pallida* showing higher basal SOD activity due zooxanthellae contributions (Main et al., 2010; Siddiqui et al., 2015). Co-exposure to Cu and low pH or salinity further amplifies antioxidant activity, reflecting integrated responses to combined oxidative and osmotic stress (Patel and Bielmyer-Fraser, 2015; Siddiqui and Bielmyer-Fraser, 2015).

Cu also inhibits carbonic anhydrase (CA) across multiple species, likely through competitive interactions with Zn at the active site (Gilbert and Guzmán, 2001; Sun et al., 2011; Patel and Bielmyer-Fraser, 2015; Siddiqui and Bielmyer-Fraser, 2015; Siddiqui et al., 2015). Interestingly, CA activity varies under co-stressor scenarios, increasing under hypo-osmotic conditions to maintain homeostasis (Gilmour, 2010; Moroney et al., 2001; Sun et al., 2011).

At the molecular level, Cu up-regulates genes associated with early stress signalling (e.g. early growth response protein 1 (*Egr1*), activator protein 1 (*AP-1*), *NF-κB*), xenobiotic detoxification (ATP-binding cassette (*ABC*) transporters, cytochrome P450 family (*CYPs*), and phytochelatin synthase 1 (*Pcs1*)), and heat-shock proteins (*HSPs*) (Elran et al., 2014), and downregulates genes involved in DNA synthesis and cellular organisation (cell proliferation and cytoskeleton), reflecting a rapid and coordinated defence strategy (Elran et al., 2014).

Collectively, these patterns underscore that Cu toxicity in sea anemones arises from complex interactions among species traits, symbiotic status, and environmental conditions.

3.2.4. Cd

Cd is a non-essential and highly toxic metal with no known biological function, and its accumulation in sea anemones is generally persistent and poorly regulated. Across species, Cd uptake and toxicity are influenced by symbiotic status, mucus production, and physiological detoxification capacity, although these factors mitigate rather than prevent bioaccumulation. Both aposymbiotic *A. equina* and symbiotic *A. viridis* show limited Cd accumulation at low exposure concentrations (5.04 μg/L), likely due to increased mucus secretion that restricts metal uptake (Harland et al., 1990). Despite this, *A. viridis* accumulates more Cd than *A. equina*, a difference attributed to Cd uptake by zooxanthellae (Harland et al., 1990). Similarly, *A. elegantissima* accumulates Cd, regardless of symbiotic state, although partitioning analyses did not reveal preferential accumulation in the algal pellet fraction, leaving the mechanism underlying symbiosis-related differences to be established (Mitchelmore et al., 2003a, 2003b). Recovery capacity following Cd exposure is limited, with both aposymbiotic and symbiotic *A. elegantissima* failing to reduce Cd levels to pre-exposure values after high accumulation (Mitchelmore et al., 2003b). Other species, such as *E. pallida* also exhibit Cd accumulation with restricted clearance capacity (Brock and Bielmyer, 2013). In contrast, *B. caissarum* accumulates Cd even at very low concentrations (0.9 μg/L), but partially mitigates toxicity through increased mucus production (Ansari et al., 2017). Overall, these studies indicate that while defensive strategies can reduce uptake rates, Cd bioaccumulation remains widespread and persistent across taxa.

Cd exerts toxic effects at multiple levels, even at low concentrations. Acute and chronic exposure studies in *Aiptasia pulchella* demonstrate high sensitivity, with 12 h-EC_{50} values ranging from 249 to 1420 μg/L (based on tentacle retraction) and a 96 h-LC_{50} of 1040 μg/L in adults (Howe et al., 2014a, 2014b, 2014c). Sub-lethal effects, such as developmental delays, reduced lacerate viability, tentacle retraction, and bleaching, occurred at lower concentrations and earlier time points, emphasising their utility as sensitive toxicity endpoints (Howe et al., 2014c). Notably, short- and long-term exposures (8–28 d) produced comparable EC_{50} values, supporting the use of *A. pulchella* as a bioindicator species. However, substantial variability in EC_{50} estimates highlights the need for methodological standardisation (e.g., anemone size, water quality, and population management).

At the biochemical level, Cd exposure triggers oxidative stress and activates enzymatic and non-enzymatic defence mechanisms. In *Bunodosoma cavernata*, Cd increases free amino acids (e.g., glutamate, alanine) levels, suggesting enhanced protein catabolism to meet energetic demands under stress (Kasschau et al., 1980). In *A. elegantissima,* Cd reduces GSH levels in aposymbiotic individuals, indicating its utilisation in detoxification, whereas symbiotic anemones maintain GSH through combined host and algal contributions, conferring greater oxidative protection (Mitchelmore et al., 2003a; Regoli and Giuliani, 2014).

Furthermore, exposure to metal mixtures (Cu, Cd, Ni, and Zn) further amplifies antioxidant responses. In *E. pallida* induced CAT and glutathione reductase (GR) activity (Brock and Bielmyer, 2013), with CAT recovering rapidly 7 d post-exposure (Brock and Bielmyer, 2013), supporting its utility as a sensitive biomarker.

At the molecular level, Cd exposure also induced the expression of stress and defence-related genes. In *N. vectensis,* 100 μg/L Cd upregulated stress-response genes (e.g., *Egr1*, *c-fos-like*, *c-jun*, and Dual-specificity protein phosphatase 1 (*Dusp1*)) and defence-related genes (e.g., *Pcs1* and *ABC* transporters), reflecting rapid activation of detoxification cascades (Elran et al., 2014). Although canonical metallothioneins appear absent in cnidarians, evidence for metallothionein-like proteins (MTLP) involvement in Cd handling has been reported in *B. caissarum* (Ansari et al., 2016), and MTLP genes are present in other species (e.g., *Actinia tenebrosa;* NCBI database ID: 116287902, Location:

NW_022258471), indicating unresolved interspecific differences in Cd detoxification strategies.

Overall, Cd toxicity in sea anemones is characterised by persistent accumulation, high-sensitivity of sublethal endpoints, and limited recovery capacity. While symbiosis can modulate oxidative defence and mitigate some toxic effects, it does not prevent Cd bioaccumulation. The pronounced influence of methodological variability and unresolved species-specific detoxification mechanisms highlights the need for standardised experimental designs and integrative biomarker approaches to improve ecological risk assessment.

3.2.5. Zn

Zn is a key essential metal for marine organisms, playing critical roles as a cofactor of several enzymes (e.g., SOD) (Mustaffa et al., 2021), in antioxidant defence (Zeinali et al., 2015), growth and development (Beltrame et al., 2010), and innate immune function (Luo et al., 2020). Its accumulation in sea anemones is influenced by the presence of symbionts. In symbiotic species such as *A. viridis*, *E. pallida*, and *A. elegantissima* (Harland et al., 1990; Mitchelmore et al., 2003b; Duckworth et al., 2017), zooxanthellae contribute significantly to Zn uptake, sometimes reaching concentrations up to 1000 times greater than host tissues (Harland et al., 1990). Conversely, aposymbiotic *A. elegantissima* accumulates lower Zn levels over time (compared to symbiotic *A. elegantissima*), due to the absence of symbionts that mediate Zn uptake (Mitchelmore et al., 2003b). Environmental factors, such as pH, can also modulate Zn accumulation as acidic pH favours the free, mobile and soluble Zn^{2+} form (Gundersen and Steinnes, 2003). Under elevated partial pressure of carbon dioxide (pCO_2) conditions (1000 pCO_2), Zn is accumulated more rapidly, suggesting increased bioavailability at lower pH (Duckworth et al., 2017).

In terms of toxicity, Zn shows relatively low acute lethality toward *A. pulchella*, with a 96 h-LC_{50} of 955 μg/L (Howe et al., 2014b). This value is higher than the 96 h-LC_{50} for more toxic metals like Cd and Pb, suggesting Zn is comparatively less acutely toxic. However, Zn toxicity increases over time, and LC_{50} values decreased from 573 μg/L at 8 d to 251 μg/L at 14 d, demonstrating notable chronic mortality (Howe et al., 2014a). Sublethal effects, including EC_{50} values, follow a similar trend, declining from 574 at 1 h to 166 μg/L at 14 d (Howe et al., 2014a and 2014b, respectively). These findings suggest *A. pulchella* is a sensitive bioindicator for Zn toxicity across life stages.

Biochemically, Zn exposure seems to impair antioxidant defences moderately. In *E. pallida*, a decrease in GR activity was observed, potentially indicating oxidative stress linked to tissue Zn accumulation (Duckworth et al., 2017). At the molecular level, Zn induced a moderate transcriptional response in *N. vectensis* (Elran et al., 2014), without a uniquely enriched pathway. However, Zn exposure activates immediate-early stress response genes (*Egr1*, *c-fos-like*, and *c-jun*) and defence-related genes (progesterone receptor membrane component (*PGRMC*), B-cell translocation 1 (*Btg1-like*), and immediate-early response proteins (*IER-domain*)), indicating that Zn elicits stress signalling patterns broadly consistent with those of other metals (Cu, Cd, and Hg).

Overall, Zn accumulation and toxicity in sea anemones are strongly affected by symbiotic status, life stage, and environmental conditions. While acute lethality is limited, chronic and sublethal effects, particularly oxidative stress, behavioural changes, and transcriptomic responses, underscore the importance of monitoring Zn in marine ecosystems and the utility of sea anemones as sensitive bioindicators.

3.2.6. Ni

Symbiotic status plays a significant role in Ni accumulation and regulation. In *A. elegantissima* and *E. pallida*, symbiotic individuals accumulate higher Ni levels than their aposymbiotic counterparts (Mitchelmore et al., 2003b; Nur et al., 2019). Partitioning studies indicate that zooxanthellae store more Ni than host tissues, possibly due to their high Ni requirements, underscoring the role of symbionts in metal regulation (Nur et al., 2019; Iyagbaye et al., 2022b). In aposymbiotic individuals, Ni can be regulated and partially eliminated over time, whereas in symbiotic anemones, Ni levels often recover to pre-exposure concentrations, further supporting the regulatory contribution of the symbionts (Mitchelmore et al., 2003b). Abiotic factors, such as lowered pH, can accelerate Ni uptake by favouring the Ni^{2+} form in more acidic waters, thereby increasing its bioavailability (Duckworth et al., 2017).

Regarding toxicity effects, Ni is relatively less lethal than other metals (e.g., Cd and Cu) with a 96 h-LC_{50} of 3980 μg/L for *A. pulchella* (Howe et al., 2014b). Chronic and sublethal exposures reveal that time is a critical factor, with the 12 h-EC_{10} of 1260 μg/L (Howe et al., 2014b) decreasing to 265 μg/L after 14 d (Howe et al., 2014a).

Biochemically, Ni can impair antioxidant defences at higher concentrations (>100 μg/L) by inhibiting GR in *E. pallida* (Duckworth et al., 2017). Short-term exposures (7 d) at environmentally relevant concentrations (10 and 100 μg/L) show minimal pH-related toxicity, suggesting effects may become more pronounced over long-term exposures (Duckworth et al., 2017). Ni also inhibits CA in species such as *C. gigantea* and *S. helianthus* after 48 h at 40 μg/L, possibly via interaction with the enzyme's active site. Exposure to extreme Ni concentrations (25 mg/L) can cause rapid mortality within 24 h (Gilbert and Guzmán, 2001), highlighting that even essential metals can pose a risk when present in excess.

Overall, while acute Ni lethality is low, sublethal and chronic-induced effects, including impaired antioxidant defences and enzymatic inhibition, highlight the importance of Ni monitoring and the value of sea anemones as sensitive bioindicators for this metal.

3.2.7. Hg

Hg is a highly toxic metal commonly found in near-shore areas, posing a major threat to sea anemones (La Corte et al., 2024). Tissue distribution studies suggest a preferential accumulation in tentacles over peduncles in *A. equina*, possibly due to their direct contact with seawater, their role in prey capture, and their interaction with suspended organic matter, which has a strong association with sediments (<63 μm) and Hg (Gadelha et al., 2010). At the physiological level, Hg alters amino acid metabolism, increasing glutamate (4-fold) and alanine (50%) levels in *A. equina* (Kasschau et al., 1980), which may reflect enhanced protein catabolism or shifts in energy production pathways as an alternative energy source during stress periods. Methylmercury (MeHg), the organic and more bioavailable form, further disrupts host metabolism in *A. viridis* through the activation of antioxidant defences (e.g., GPx activity) and the induction of alkaline phosphatase (ALP) activity (La Corte et al., 2024), a response often associated with detoxification and membrane repair. MeHg exposure also reduces lysozyme (LYS) activity in *A. viridis*, suppressing immune defence, and potentially increasing susceptibility to other infections and stressors (La Corte et al., 2024). Under combined exposure to MeHg and *Escherichia coli*, oxidative stress responses were amplified (e.g., GPx and esterase (EST) activity), while MeHg continued to suppress immune function by downregulating LYS production, suggesting that multiple stressors exacerbate cellular redox imbalance while weakening host immunity (La Corte et al., 2024). Behaviourally, MeHg can cause reduced motility and turgidity in sea anemones, consistent with systemic toxicity and impaired homeostasis (Lee et al., 2020).

At the molecular level, Hg has a massive effect on *N. vectensis*, ranking as the most toxic among tested metals (Cd, Cu, Zn, and Hg) (Elran et al., 2014). Transcriptomic analyses revealed rapid activation of defence pathways, including immediate early response genes (*Egr1*, *c-fos-like*, *c-jun*), transcriptional regulators (*AP-1* complex, *NF-κB*), stress-related genes (*Hsp20*, *Hsp70*, and *ABC* transporters), and detoxification enzymes (*Pcs1*, *CYPs*, and glutathione *S*-transferases (*GST*)) (Elran et al., 2014). In contrast, Hg downregulated genes involved in DNA replication, cytoskeletal organisation (microtubules), and ion transporters, indicating a reallocation of cellular energy away from growth and housekeeping functions toward defence and detoxification (Elran et al., 2014).

Taken together, these findings highlight the extreme toxicity of Hg to sea anemones, with effects spanning from altered amino acid metabolism and oxidative stress responses to immune suppression, behavioural impairment, and profound transcriptomic reprogramming.

3.2.8. Mn

Mn accumulation in sea anemones has been shown to occur in both host tissues and their symbionts (Iyagbaye et al., 2022a, 2022b). Additionally, zooxanthellae accumulate up to 20-fold more Mn than host tissue, with a reported bioconcentration factor (BCF) of 859 compared to 42 in *E. pallida* tissue (Iyagbaye et al., 2022a). This preferential accumulation by symbionts may reflect both a higher affinity for Mn and its essential role in photosynthetic processes, particularly within photosynthesis II (Biscéré et al., 2018). In mixed exposures with Ni and Mn, accumulation remained primarily driven by Mn availability, indicating limited interaction between these metals in terms of uptake (Iyagbaye et al., 2022b). Despite its high accumulation, *E. pallida* have some capacity to regulate Mn, as concentrations declined during 6 d recovery period, though levels remained above baseline (Iyagbaye et al., 2022a, 2022b). Long recovery times may therefore be required for full depuration.

Toxicity studies suggest that Mn is less acutely harmful than other metals. For *E. pallida*, the 96 h-LC_{50} decreased from 141 to 102.9 mg/L after 10 d of exposure (Iyagbaye et al., 2022a). In contrast, no lethal or sublethal effects were reported in small *E. pallida* (1 to 5 mm) exposed to up to 60 mg/L of Mn for 12 d (Summer et al., 2019), suggesting relatively high short-term tolerance. Nevertheless, considering chronic exposure scenarios, Mn could pose a significant hazard. At sublethal levels, Mn accumulation did not reduce symbiont density at concentrations up to 100 mg/L (Iyagbaye et al., 2022a, 2022b). This tolerance may be linked to the functional role of Mn in photosynthesis II (Biscéré et al., 2018) and its function as cofactor of SOD, an antioxidant enzyme shown to be altered by Mn exposure in other dinoflagellate models (Cao et al., 2011). However, when co-exposed to Ni, symbiont density declined, presumably due to enhanced oxidative stress and disruption of host-symbiont dynamics, ultimately leading to bleaching (Iyagbaye et al., 2022b). This suggests that combined metal exposure (Mn + Ni) exacerbates toxicity, possibly through Mn overload or interference with redox regulation.

Tentacle retraction was consistently observed in *E. pallida* under both Mn alone and Mn + Ni exposure, indicating this as a sensitive endpoint for evaluating Mn toxicity (Iyagbaye et al., 2022a, 2022b). One possible explanation is that Mn would disrupt neuromuscular function, as it is a well-known neurotoxicant that can interfere with calcium-regulated ion channels in marine invertebrates (Deidda et al., 2021). However, the pathway underlying tentacle retraction in cnidarians remains unresolved, and further research is needed to unravel whether neuromuscular disruption is a result of metal toxicity in sea anemones. Beyond being a defensive reaction, tentacle retraction also plays key roles in host-symbiont interactions by reducing light availability for zooxanthellae, potentially impairing photosynthesis and leading to energy deficits. Prolonged retraction, in turn, compromises feeding and may ultimately lead to death.

Overall, Mn exhibits a dual nature in sea anemones: (1) while essential for symbiont metabolism and tolerated at relatively high levels, (2) excessive accumulation, especially in combination with other metals, triggers oxidative stress, behavioural disruption, and potential bleaching, emphasising the need to consider both concentration and co-exposure scenarios in assessing Mn hazard.

3.2.9. Al, Co, Pb, and V

No laboratory studies were found that assessed the accumulation of Al, Co, Pb, and V in sea anemones. The available evidence is therefore limited to ecotoxicological endpoints. For Al, toxicity to *E. pallida* appears relatively low, with a 14d-EC_{50} of 2270 μg/L (Trenfield et al., 2017). The effect of temperature fluctuations (± 3/4 °C) on Al toxicity was explored but remains unclear. While reproductive output decreased under these suboptimal conditions, the role of AI speciation changes driven by physicochemical dynamics may mask or modulate the toxicity of AI (Trenfield et al., 2017).

Co displayed relatively low lethality in *A. pulchella*, with a 14d-LC_{50} of 601 μg/L (Howe et al., 2014a, 2014b). However, sublethal endpoints were far more sensitive. Tentacle retraction produced a 96 h-EC_{50} of just 27 μg/L, whereas reproductive endpoints were less sensitive, with EC_{50} values of 561 μg/L (14 d) and 107 μg/L (28 d) (Howe et al., 2014b). These findings highlight the greater sensitivity of behavioural endpoints compared to developmental ones. In addition, Co exposure induced extreme bleaching and mucus production, regardless of concentration (Howe et al., 2014a, 2014b). These responses represent defensive strategies, expulsion of zooxanthellae to limit Co accumulation, and mucus secretion to reduce further uptake via skin adsorption.

Pb also demonstrated low lethality in *A. pulchella*, with a 96 h-LC_{50} of ~10,230 μg/L and a 12 h-EC_{50} of 1740 μg/L (Howe et al., 2014b). These thresholds suggest greater tolerance compared to many marine invertebrates (Botté et al., 2022). Massive bleaching was triggered at ≥688 μg/L, which may represent a key detoxification strategy, reducing Pb accumulation in symbionts and minimising toxicity at the organismal level (Howe et al., 2014b). Despite these high-effect thresholds, biochemical assays revealed Pb sensitivity at much lower concentrations, CA activity was inhibited at only 40 μg/L in *C. gigantea* and *S. helianthus* (Gilbert and Guzmán, 2001). This demonstrates that Pb can significantly impair cellular functions at concentrations well below those causing visible effects.

Similarly, V was shown to strongly inhibit CA activity at concentrations >20 μg/L in *C. gigantea* and *S. helianthus*. Given the key role of CA in calcification, pH regulation, and photosynthetic carbon supply, V exposure could disrupt host-symbiotic interactions, with broader consequences for holobiont health (Gilbert and Guzmán, 2001). Collectively, these results reinforce CA as a sensitive biomarker for metal stress, capable of revealing sublethal effects (e.g., Cu, V, Pb, and Ni) even when whole-organism responses appear muted.

4. Conclusions, current gaps, and future perspectives

This study provides the first systematic review of metal accumulation patterns and associated ecotoxicological effects in sea anemones in both field and laboratory contexts. In approximately 20 metals studied so far, it was noted that sea anemones are broad-spectrum metal accumulators, with Fe and Ba most frequently reaching the highest tissue concentrations,. Among tissues, the pedal disk emerged as a potential key site for assimilation and storage (e.g., Fe, Ba, Al, Zn, and Sr), although evidence remains limited. Accumulation patterns are primarily driven by environmental metal bioavailability and symbiotic state. Hydrothermal systems showed the highest accumulation levels across all evaluated metals, and symbionts appear to act as major accumulators for specific metals (e.g., Cu and Fe). In laboratory studies, *E. pallida* dominated as the bioindicator model species, and across taxa a consistent dose- and time-dependent accumulation pattern was observed for most of the studied metals (e.g., Cu, Cd, Zn, Ni, and Mn). Both abiotic (e.g., temperature, salinity, and pH) and biotic factors (e.g., size and symbiotic state) modulate metal uptake. Biological effects span multiple levels of organisation, from molecular to organismal responses, including transcriptome reprogramming, oxidative stress, altered detoxification, DNA damage, immune suppression, cytotoxicity, metabolic and cellular disruption, impaired reproduction and development, loss of zooxanthellae and tentacles, swelling, and tentacle retraction. Together, these findings support the suitability of sea anemones as sensitive models for ecotoxicology, while also highlighting substantial gaps that currently limit their broader application.

4.1. Methodological limitations

Methodological heterogeneity represents a significant barrier to cross-study synthesis. Experimental designs vary widely in organism density, size, life stage, and key abiotic parameters (pH, temperature, and salinity), hindering quantitative comparisons. Tissue selection is not standardised, and tissue-partitioning analyses are still scarce, resulting in inconsistent identification of accumulation target tissues. In addition, metal concentration is often reported using different units (dw vs. ww), further complicating comparisons. Long-term exposures ($\geq$ 28 d), mechanistic mixture experiments, and post-exposure recovery or depuration phases remain scarse, despite evidence that several metals exhibit toxicity only after prolonged exposure. Multi-stressor experiments integrating metals with climate-related drivers (e.g., warming, acidification, salinity changes) also remain underexplored.

4.2. Mechanistic gaps

Mechanistic understanding of both single-metal and environmentally realistic mixture exposures, including interaction types (e.g., additivity, antagonism, synergy) are still poorly characterised. The primary tissues responsible for metal assimilation and long-term storage remain unresolved due to a lack of standardised, tissue-specific analyses, although the pedal disk appears to have a crucial role. The contribution of symbionts in metal uptake, regulation, and storage remains poorly characterised, as does the extent to which bleaching functions as a regulatory or protective response. Importantly, the consequences of symbiotic-mediated metal handling for host antioxidant systems, detoxification capacity, and overall fitness remain unclear across species, metals, and environmental conditions.

4.3. Ecosystem and sampling gaps

Research effort is geographically concentrated in a limited number of countries (notably the United States, Australia, Spain, and Brazil), leaving major knowledge gaps in polar, deep-sea, and underrepresented coastal systems. Field studies that directly link metal accumulation to in situ biological effects are particularly scarce. This lack of ecological validation constrains our ability to extrapolate laboratory findings to natural systems and limits the development of robust, ecosystem relevant risk assessments.

4.4. Biomarker and omics gaps

While several biomarkers have been studied (e.g., antioxidant enzymes, carbonic anhydrase, genotoxicity endpoints), their specificity, standardisation, and validation across taxa and environments remain limited. High-throughput omics approaches (transcriptomics, proteomics, metabolomics) are still underused in sea anemone metal ecotoxicology, despite their strong potential to identify early, metal-specific responses and to support the development of robust, multi-endpoint biomarker panels.

4.5. Research priorities

To consolidate sea anemones as models for metal ecotoxicology and environmental monitoring, future research should prioritise experiments with well defined biotic and abiotic parameters, using environmentally realistic concentrations, and with sufficient replication. Metal accumulation should be reported in μg/g of dry weight, ideally alongside water content to allow conversion to wet weight, and complemented by standardised bioaccumulation metrics (e.g., BCF). Long-term exposure and recovery experiments, as well as multi-stressor designs integrating metals with climate-related drivers (pH, temperature, and salinity), should be prioritised. Pedal disk, column, and tentacles should be considered the preferred target tissues for metal accumulation analyses, ideally coupled with metal speciation, a critical determinant of bioavailability and toxicity. Mechanistic studies addressing the role of symbiosis across taxa, metals, and environmental conditions are urgently needed. Finally, field studies employing robust sampling strategies that link accumulation to multi-biomarker responses (e.g., oxidative stress, neurotoxicity, genotoxicity, and metal detoxification) and omics approaches will be essential for biomarker identification and validation. Collectively, these efforts will strengthen the ecological relevance of laboratory findings and enhance the use of sea anemones species as bioindicators for environmental risk assessment and/or monitoring programs.

CRediT authorship contribution statement

Juliano M. Vilke: Writing – review & editing, Writing – original draft, Visualization, Software, Methodology, Formal analysis, Conceptualization. **Deborah M. Power:** Writing – review & editing. **Cármen S. V. de Sousa:** Writing – review & editing, Writing – original draft, Supervision, Conceptualization. **Nélia C. Mestre:** Writing – review & editing, Writing – original draft, Supervision, Funding acquisition.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Nelia Mestre reports financial support was provided by Foundation for Science and Technology. Juliano Vilke reports financial support was provided by Foundation for Science and Technology. Nelia Mestre reports a relationship with Federal Institute for Geosciences and Natural Resources that includes: consulting or advisory. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.marpolbul.2026.119241.

Data availability

No data was used for the research described in the article.

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