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Advances and Engineering Strategies in Microalgae-Based Heavy Metal Bioremediation

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Abstract

Heavy metal (HM) contamination represents a persistent global challenge due to its toxicity, persistence, and bioaccumulative nature, often exacerbated by anthropogenic activities such as industrial effluent discharge, mining, and fossil fuel combustion. Conventional remediation methods—including chemical precipitation, ion exchange, and electrochemical treatments—are limited by high operational costs, inefficacy at low metal concentrations, and secondary waste generation. In contrast, microalgae-based bioremediation offers a biologically sustainable and economically viable alternative. Microalgae possess cell wall polysaccharides and metal-binding functional groups that facilitate biosorption, while their metabolic adaptability allows them to thrive in variable wastewater conditions. Moreover, recent advances in genetic and metabolic engineering have enhanced metal uptake specificity, resistance to toxicity, and biotransformation capacity. Immobilization techniques and cultivation system innovations (e.g., photobioreactors) have further improved their operational stability and scalability. Importantly, post-remediation valorization of algal biomass into biofuels or bioproducts supports circular bioeconomy principles. This review critically synthesizes recent developments in microalgae-mediated HM remediation, highlighting mechanistic insights, bioengineering innovations, and implementation challenges. By outlining current gaps and proposing integrative strategies, this review provides a roadmap for translating laboratory-scale findings into effective environmental technologies.

Keywords: Microalgae, Phycoremediation, Pollution, Genetic engineering, Water treatment

Introduction

Heavy metal (HM) contamination has become a critical and persistent threat to aquatic ecosystems and human health due to the non-biodegradable nature, bioaccumulation, and trophic magnification of these elements. Essential metals (e.g., Zn, Cu, Fe) and non-essential toxic metals (e.g., As, Pb, Hg, Cd, Cr) are continuously introduced into water bodies through industrial effluents, mining and smelting activities, fossil fuel combustion, agricultural runoff, and domestic wastes such as paints, batteries, and pharmaceuticals. In parallel, geogenic processes including bedrock weathering and acid mine drainage further mobilize metals into surface and groundwater [1]. These overlapping anthropogenic and natural inputs generate complex multi-metal and multi-pollutant mixtures that accumulate in sediments and biota, disrupt ecological functions, and pose long-term health risks, particularly in vulnerable regions with limited wastewater treatment capacity [2,3]. As regulatory thresholds become more stringent and monitoring reveals increasing HM burdens in aquatic systems, the development of remediation strategies that are efficient, scalable, and environmentally sustainable has become an urgent global priority [4].

Conventional physicochemical techniques, such as chemical precipitation, ion exchange, membrane filtration, electrochemical treatment, and coagulation-flocculation have been widely adopted for HM removal from wastewater [5]. While these technologies can achieve high removal efficiencies under controlled conditions, they are frequently constrained by high energy and chemical demand, declining performance at low metal concentrations, and the generation of toxic sludge that requires further management or disposal. Moreover, their performance often decreases in complex effluents containing mixtures of metals, nutrients, and organic contaminants that alter metal speciation and interfere with removal processes [1,6]. These constraints have driven increasing interest in biological and nature-based alternatives capable of addressing complex metal mixtures while minimizing secondary pollution, particularly those that are sustainable, cost-effective, and capable of treating complex metal mixtures in real-world settings.

Microalgae have emerged as highly promising platforms for HM bioremediation in aquatic environments because they couple contaminant removal with biomass production and resource recovery. Their polysaccharide-rich cell walls provide abundant functional groups (carboxyl, hydroxyl, sulfate, phosphate, amine) that support rapid extracellular biosorption via ion exchange, chelation, electrostatic attraction, and physical adsorption, forming an effective first line of defense against metal toxicity. Complementary intracellular mechanisms include energy-dependent transport of metal ions into the cytoplasm, vacuolar sequestration, chelation by glutathione, phytochelatins (PCs), and metallothioneins (MTs), and enzymatic biotransformation of highly toxic species (e.g., Cr(VI), Hg^{2+}, inorganic As) into less harmful forms. These pathways enable microalgae to tolerate and detoxify a wide range of metals across diverse exposure scenarios, from concentrated industrial discharges to diffuse agricultural runoff, and to function in both single-metal and complex multi-metal systems [6,7]. Moreover, unlike bacterial systems, microalgae contribute to wastewater oxygenation and chemical oxygen demand (COD) reduction, enhancing overall treatment efficacy [8]. Recent evidence also shows that microalgae can tolerate and transform mixed-metal contaminants, underscoring their potential suitability for real-world wastewater streams [5-7].

Further advantages include the rapid development of genetic, metabolic, and adaptive engineering tools, which allows microalgal strains to be tailored with improved uptake capacities, metal specificity, and resistance to metal-induced oxidative stress [7,8]. In recent years, innovations such as CRISPR-based gene editing, multi-omics-guided strain selection, transporter engineering, advanced photobioreactor (PBR) optimization, and microalgal immobilization matrices have significantly enhanced system stability, uptake performance, and operational scalability. These developments further expand the integration potential of microalgae into continuous-flow systems and industrial wastewater treatment infrastructures [9]. In addition, the valorization of microalgal biomass into high-value products (e.g., biofuels, bioplastics, feed additives) supports circular bioeconomy initiatives, thereby improving process economics and sustainability [7,10].

However, despite these advances, critical knowledge gaps remain particularly in strain-specific variability, multi-metal remediation, techno-economic performance, and the long-term environmental sustainability of engineered microalgal systems. To address these gaps, this review synthesizes recent developments in microalgae-based heavy metal bioremediation, highlighting cellular and molecular mechanisms, engineering strategies, emerging technologies, and challenges related to scalability. By integrating insights from genetics, environmental biotechnology, and bioprocess engineering, this review outlines future research directions toward next-generation phycoremediation systems capable of efficient deployment in real-world heavy metal-contaminated environments.

Heavy metal contamination in aquatic environment

Heavy metals (HMs), including essential elements (e.g., Zn, Cu, Fe) and non-essential toxic metals (e.g., As, Pb, Hg, Cd, Cr), pose persistent threats to aquatic ecosystems and human health due to their bioaccumulative and trophically magnified nature

[11,12]. Contamination arises from multiple, overlapping pathways: Industrial effluents, mining, smelting, and agricultural runoff introduce metals such as As, Ni, Cu, Cd, and Pb, while domestic wastes (paints, batteries, pharmaceuticals) often bypass municipal treatment [13-15]. Natural geogenic processes, including bedrock weathering and acid mine drainage, further amplify metal mobilization [14,16]. This complex, multi-source contamination challenges conventional mitigation strategies and demands adaptive solutions.

Microalgae offer a unique advantage: Their metabolic versatility enables targeted uptake and detoxification across diverse contamination scenarios, from concentrated industrial discharges to diffuse agricultural runoff. Integrating microalgae-based strategies into monitoring and remediation frameworks provides a sustainable, scalable approach to managing both acute and chronic HM pollution [17,18]. **Table 1** provides a comparative assessment of five major heavy metals commonly found in contaminated water systems. The table summarizes their representative sources, primary health effects, environmental behavior, and critical concerns, offering insights for prioritizing remediation efforts and risk assessment framewor.

Table 1 Comparative assessment of major heavy metals: sources, toxicological relevance, and environmental concerns.

Heavy metal	Representative sources	Primary toxicological effect	Regulatory limit (mg/L)	Environmental concern	Critical remarks	Ref.
Arsenic (As)	Mining, pesticides, semiconductors	Carcinogen, dermal toxicity	0.05	Persistent in groundwater	Major risk in South East Asia aquifers	[17,18]
Lead (Pb)	E-waste, plumbing, fuels	Neurotoxic, reproductive damage	0.05	Sediment accumulation	Affects children's development	[19-21]
Mercury (Hg)	Coal burning, industry, batteries	Kidney & CNS toxicity	0.00003	Bioaccumulation in fish	Critical in trophic magnification	[18,22]
Cadmium (Cd)	Fertilizers, plating, batteries	Renal dysfunction, bone damage	0.01	Mobile in acidic soil	High uptake in crops	[18,21,23]
Chromium (Cr VI)	Leather, dyeing, electroplating	Carcinogenic, dermal ulceration	0.05	Soluble, highly mobile	Requires reduction to Cr(III)	[21,24,25]

As shown in **Table 1**, metals like mercury and cadmium are particularly problematic due to their bioaccumulative nature and mobility in acidic conditions, respectively. Lead poses long-term ecological risks due to its persistence in sediments and its neurotoxic effects, especially on children. Chromium (VI), despite having regulatory limits similar to arsenic and lead, is highly mobile and carcinogenic, necessitating its reduction to the less toxic Cr(III) form prior to remediation [24,25]. These distinctions underscore the need for microalgal strains with metal-specific uptake pathways, tolerance thresholds, and detoxification mechanisms. Moreover, real aquatic environments rarely contain single metals; instead, they present complex mixtures of heavy metals, pesticides, pharmaceuticals, and organic pollutants, which can exert synergistic or antagonistic toxic effects [15]. Microalgae capable of multi-contaminant tolerance through biosorption, intracellular sequestration, enzymatic degradation, or reactive oxygen species (ROS)-mediated detoxification that are particularly valuable in treating realistic wastewater matrices [26].

Despite these advantages, real-world implementation of microalgae-based bioremediation faces challenges, including scalability, light availability, contamination in open systems, biomass harvesting costs, and fluctuating wastewater chemistry [18]. Addressing these constraints requires engineered photobioreactors, integrated hybrid systems, and improved strains developed through adaptive evolution or genetic engineering. Microalgae can also be embedded within broader pollution-monitoring frameworks, functioning as both bioremediators and biosensors whose physiological responses (e.g., chlorophyll fluorescence) indicate metal stress in real time [27]. Additionally, the practical benefits of microalgae such as low energy demand, nutrient recycling, CO_2 utilization, and biomass valorization into biofuels or high-value bioproducts position them as a sustainable and increasingly attractive alternative to conventional treatment technologies [28]. These integrated perspectives on pollution sources, metal characteristics, multi-contaminant interactions, and implementation challenges provide a foundational basis for advancing engineered microalgae-based bioremediation strategies that are adaptive, cost-effective, and aligned with real-world environmental management needs.

Mechanism of heavy metal uptake by microalgae

Microalgae utilize multiple complementary mechanisms to mitigate the toxicity of HM, enabling them to survive and thrive in contaminated aquatic systems. These mechanisms operate at both extracellular and intracellular levels, and their effectiveness depends on environmental conditions, metal speciation, and the physiological traits of the algal strain. In practical applications, the efficiency of these mechanisms also depends on how well they can be integrated into engineered systems such as photobioreactors, fixed-bed biosorption columns, and immobilized-biomass reactors to achieve scalable and economic wastewater treatment [9,10,21]. Extracellular mechanisms include ion exchange, electrostatic attraction, chelation by cell wall polysaccharides, and physical adsorption to functional groups such as carboxyl, hydroxyl, and phosphate groups. These interactions enable rapid initial binding of metal ions and often serve as the first line of defense. Intracellular mechanisms involve the active transport of metal ions into the cytoplasm, followed by sequestration into vacuoles, binding with PCs or MTs, and in some cases, enzymatic biotransformation into less toxic forms. This intracellular processing provides long-term detoxification and prevents interference with essential cellular processes [29].

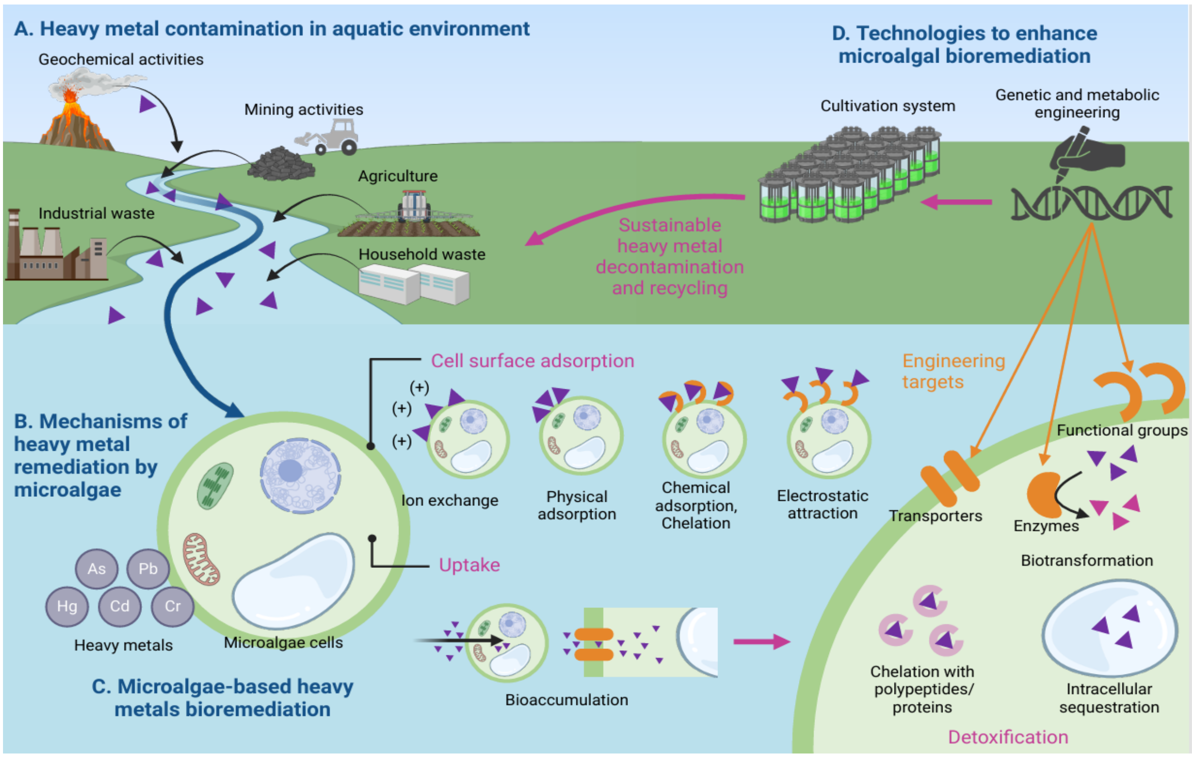

Figure 1 Conceptual framework of microalgae-based heavy metal bioremediation: (A) major sources of heavy metal contamination in aquatic environments, (B) extracellular and (C) intracellular mechanisms employed by microalgae for metal removal, and (D) technological strategies to enhance bioremediation via cultivation and genetic engineering.

Although these mechanisms have been well characterized, their real-world relevance depends significantly on strain-specific physiological variability, which determines both adsorption efficiency and detoxification capacity. For example, *Chlorococcum dorsiventrale* removes chromium through a combined extracellular–intracellular mechanism but removes lead almost exclusively via membrane adsorption, achieving 89% and 95% removal, respectively [30]. Hyper-accumulator species such as *Spirulina* sp., *Chlorella* spp., and *Scenedesmus* spp. exhibit superior performance in acid-mine drainage environments, where they remove metals simultaneously via surface adsorption and intracellular bioaccumulation. Other species such as *Phaeodactylum tricornutum* demonstrate high metal selectivity, highlighting the importance of informed strain selection when designing industrial remediation systems [31]. Both living and non-living biomass have been employed, where live cells support dynamic detoxification while non-living biomass offers rapid passive removal without the need for illumination [32].

Figure 1 illustrates the comprehensive pathway of heavy metal contamination and the corresponding microalgal bioremediation strategies. Panel A depicts major sources of HM pollution in aquatic environments, including industrial discharge, mining runoff, agricultural chemicals, and household waste. Natural processes such as weathering and geochemical leaching may further mobilize metals into water systems. Panel B and C summarize the key mechanisms by which microalgae mitigate heavy metal toxicity. These include extracellular interactions, such as ion exchange, physical and chemical adsorption, chelation, and electrostatic attraction, which allow rapid binding of metal ions at the cell surface. Once internalized, metals are further managed through bioaccumulation, intracellular sequestration, and binding with polypeptides or proteins (PCs or MTs). These processes prevent disruption of cellular homeostasis and support long-term detoxification. Panel D highlights emerging technological strategies to enhance microalgal remediation efficiency, including the development of optimized cultivation systems (e.g., photobioreactors) and genetic and metabolic engineering. Such engineering approaches include transporter overexpression, enhanced PCs/MTs biosynthesis, and suppression of toxic biotransformation pathways, all of which are highly relevant to industrial wastewater treatment. These approaches are aligned with the principles of sustainable wastewater treatment and circular bioeconomy by enabling resource recovery alongside decontamination. The detailed mechanisms discussed in Panels B and C are further elaborated in the following sections (3.1 and 3.2), providing insights into how microalgae differentially respond to and process various heavy metals.

Extracellular mechanisms

The initial defense of microalgae against HM occurs at the cell surface through extracellular mechanisms that passively immobilize metal ions prior to cellular entry [33]. These mechanisms are largely governed by the biochemical composition and surface chemistry of the microalgal cell wall, which contains abundant polysaccharides, proteins, and lipids rich in functional groups such as carboxyl (–COOH), hydroxyl (–OH), sulfate ($–SO_4^{2-}$), phosphate ($–PO_4^{3-}$), and amine ($–NH_2$) [30]. Variability in the density and distribution of these groups across strains produces substantial differences in biosorption capacity and metal selectivity, making strain choice a critical design parameter for industrial bioremediation applications. One dominant pathway is ion exchange, in which HM in the surrounding medium displace endogenous cations (e.g., Ca^{2+}, Mg^{2+}) previously bound to negatively charged sites on the cell wall. The efficiency of this mechanism depends on metal affinity, ionic radius, and solution pH. Metals like Pb^{2+} and Cd^{2+} show high displacement potential due to stronger binding affinity to carboxyl and sulfate moieties. However, competition among metal ions and limited exchange sites may restrict uptake under complex wastewater conditions [34].

Chelation, another key extracellular process, involves the formation of stable coordinate bonds between metal ions and electron-donating ligands on the microalgal surface [26]. Functional groups such as –COOH and –OH serve as primary chelation sites. Chelate formation improves the thermodynamic stability of bound metals and reduces their bioavailability and toxicity, although irreversible binding may hinder recovery and recycling efforts [29,35]. In parallel, electrostatic attraction facilitates the surface accumulation of cationic metal species (e.g., Cr^{3+}, Cu^{2+}) by interacting with negatively charged cell wall domains [36]. This mechanism is most effective under neutral to slightly acidic pH, where deprotonated functional groups are prevalent. However, ionic strength and the presence of competing ions can diminish its efficiency [29,36].

Physical adsorption, driven by weak van der Waals forces or hydrogen bonding, provides an additional layer of surface retention [35]. Although less specific and less stable than chemisorption, this mechanism allows for rapid and reversible metal immobilization, which can be beneficial in dynamic remediation systems. The surface area, cell wall porosity, and functional group density strongly influence adsorption capacity [37]. These extracellular mechanisms are also the most technologically scalable because they remain functional even in non-living biomass. As a result, they form the basis of industrial biosorption systems, including fixed-bed reactors, membrane-assisted sorption units, and rotating algal biofilms, enabling low-cost and low-energy treatment of complex wastewaters. Hyper-adsorbent strains such as *Spirulina* sp., *Chlorella* sp., and *Scenedesmus* sp. have therefore become primary candidates for industrial deployment in systems such as acid mine drainage treatment [31].

Intracellular mechanisms

After the initial extracellular immobilization, microalgae initiate a second phase of detoxification through intracellular mechanisms, allowing long-term regulation of metal ions. This process, known as bioaccumulation, begins with the energy-dependent transport of metal ions into the cytoplasm through specific membrane transporters (e.g., ZIP, NRAMP, ABC transporters). These proteins facilitate the selective uptake of metal ions such as Cd^{2+}, Pb^{2+}, and Hg^{2+}, often against concentration gradients, using ATP as an energy source [38]. Transporter expression levels differ widely across species, explaining why some strains exhibit greater tolerance or intracellular detoxification capacity than others [27,38].

Once internalized, metals are frequently sequestered in vacuoles, effectively isolating them from sensitive cellular machinery [39]. This compartmentalization minimizes cytoplasmic toxicity and prevents interference with enzymatic and metabolic processes. To further detoxify these ions, microalgae synthesize low-molecular-weight metal-binding peptides, including PCs and MTs. These molecules chelate metal ions via thiol groups, forming stable metal–peptide complexes that can be safely stored or trafficked within the cell [27,40]. Notably, species such as *Chlorella vulgaris* and *Scenedesmus obliquus* show strong induction of PCs/MTs biosynthetic pathway, whereas *Spirulina* sp. demonstrates a weaker PC/MT response and relies more on extracellular adsorption, making it less effective for intracellular-driven remediation [27]. Recent work also shows that certain microalgae can naturally evolve enhanced intracellular tolerance to specific metals; for example, a chromium-resistant strain (CRS) exhibited strong upregulation of antioxidant enzymes (superoxide dismutase, catalase) and improved redox homeostasis, enabling efficient mitigation of Cr(VI)-induced oxidative stress through reinforced intracellular chelation and detoxification [41].

Some species also possess the ability to biotransform metals through enzymatic modification, providing both advantageous and potentially harmful outcomes. Chromate reductases convert carcinogenic Cr(VI) to Cr(III), while mercuric reductase reduces Hg^{2+} to elemental Hg^0 [42]. However, certain microalgae and associated microbiota can methylate Hg^{2+} into methylmercury (MeHg), a highly toxic and bioaccumulative compound, representing a major ecological and human health risk [29,42]. Thus, strains capable of mercury methylation require strict biosafety evaluation or targeted genetic modification to suppress methylation pathways before being considered for environmental applications [42].

While intracellular mechanisms enhance detoxification depth, they impose metabolic burdens that may reduce biomass productivity. This metabolic cost underscores the importance of selecting strains with efficient vacuolar sequestration and balanced redox physiology [29,37]. For instance, *Nannochloropsis sp.* possesses robust vacuolar compartmentalization that enables storage of large quantities of metal–peptide complexes with minimal growth inhibition, making it suitable for high-rate photobioreactors.

Biotechnological strategies have increasingly been employed to enhance these pathways. Adaptive laboratory evolution (ALE) has successfully improved transporter expression and metal tolerance [43], while CRISPR-based editing has enabled precise modification of PCs/MTs biosynthetic gene to increase chelation capacity. Genetic suppression of mercury-methylation pathways has also shown promise in reducing MeHg formation without compromising detoxification ability. When these engineered traits are integrated with optimized photobioreactor lighting, bicarbonate-enhanced CO_2 delivery, and algal–bacterial consortia, intracellular processing can be significantly improved while maintaining high biomass productivity [44].

In addition to understanding the biological mechanisms of metal uptake, rigorous monitoring and standardized performance metrics are essential to accurately evaluate microalgal heavy-metal removal efficiency in both laboratory and pilot-scale systems. Commonly applied indicators include maximum adsorption capacity (q_e, mg g^{-1} dry biomass), removal efficiency (%), uptake rate (mg g^{-1} h^{-1}), and tolerance thresholds such as EC_{50}, which collectively describe the biosorption potential, kinetic behaviour, and physiological sensitivity of microalgae under metal stress [6,7,18]. Reliable analytical techniques are equally fundamental: Inductively coupled plasma–based methods (ICP-MS/ICP-AES) are widely used for precise metal quantification in water and biomass [45], while FTIR and XPS provide insight into cell-wall functional groups and binding chemistry at the microalgal surface [46]. Subcellular metal localization and the distinction between surface adsorption and true intracellular accumulation can be resolved using electron microscopy coupled with EDX, particularly in biofilms and immobilized systems [47]. In parallel, omics-based tools, including transcriptomics and proteomics have been increasingly applied to map stress-responsive pathways and transporter regulation in metal-exposed microalgae, thereby linking molecular responses with observed detoxification performance and biomass productivity [48,49].

Recent advance of microalgae-based heavy metal bioremediation

Arsenic bioremediation

Arsenic contamination poses severe risks to aquatic ecosystems due to its high mobility, persistence, and speciation-dependent toxicity. Microalgae offer a promising biological solution for arsenic (As) remediation through a combination of extracellular adsorption, intracellular transformation, and metabolic detoxification mechanisms. Microalgae can modulate the toxicity of inorganic As species, notably by oxidizing As(III) to the less toxic As(V) and reducing As(V) for subsequent intracellular processing. Key detoxification routes include chelation with glutathione and phytochelatins, extracellular complexation, and methylation into organoarsenicals (e.g., arsenolipids, arsenosugars), some of which may be excreted [50]. These reactions occur via interactions with surface functional groups such as –OH, –NH, –CN, and aldehyde-based moieties, or through enzyme-mediated pathways [51].

Table 2 summarizes recent advances in As bioremediation using diverse microalgal taxa. Strains from the genera *Chlorella*, *Chlamydomonas*, *Scenedesmus*, and *Nostoc* have shown effective As uptake, with efficiencies ranging from 30% - 95% depending on species, initial concentration, and environmental parameters [52-55]. Notably, *Chlamydomonas sp.* achieved 95.2% removal efficiency at 200 mg/L As under 60 min of exposure, reflecting robust biosorption and transformation capacity [46]. Adsorption behaviors in several studies were best described by pseudo-second order kinetics and Langmuir isotherms, indicating spontaneous and monolayer adsorption mechanisms [56].

Hybrid systems integrating microalgae with engineered materials, such as nano-zero valent iron (NZVI), have further enhanced arsenic removal performance. For instance, *Chlorella vulgaris* combined with NZVI achieved up to 99% removal, with thermodynamic analyses confirming a physisorption-dominated mechanism [57]. This reflects an emerging trend in coupling biological and nanomaterial approaches for high-efficiency bioremediation. Recent findings also underscore the role of environmental cofactors in modulating arsenic uptake. The presence of phosphate and other competing anions significantly affects metal speciation and transport. Comparative studies on *Nostoc NIES-2111_MUM004* and *Chlorella sorokiniana MUM002* revealed that phosphate depletion can enhance arsenic bioaccumulation, particularly in cyanobacteria, which regulate specific arsenic-related gene expression pathways [58].

Recent studies have begun exploring strain-level engineering to enhance arsenic tolerance and uptake, including the characterization of arsenate reductase in *Chlamydomonas* and its role in As(V)/As(III) biotransformation [59,60], as well as the identification of As-related genes and enzymes involved in redox conversion and methylation pathways in diverse microalgae [50,61]. Genetic modification of microalgal strains to overexpress detoxification-related enzymes and transporters has been reported to substantially improve arsenic removal compared to wild-type counterparts [61]. In parallel, ALE has emerged as a powerful strategy to obtain microalgal variants with enhanced stress tolerance and improved metal detoxification capacity, including tolerance to metalloid and heavy-metal stress [43,62].

From a technological perspective, scalable implementation of As bioremediation will require low-energy systems such as biofilm or hybrid algal–material reactors, integrated with resource recovery (e.g., nutrient or biomass valorization) to improve economic viability. Recent techno-economic assessments (TEA) of microalgae-based wastewater polishing and heavy-metal removal show that cultivation and harvesting costs can be offset when biomass is valorized for co-products such as biofertilizers or lipids [63-65]. At the same time, As methylation and volatilization by microalgae can generate organoarsenicals with uncertain long-term environmental behavior, highlighting the need for closed or semi-enclosed photobioreactors and careful monitoring of gaseous emissions in pilot and full-scale systems [50,66].

Table 2 Recent advances in Arsenic bioremediation using microalgae.

Microalga strains	(As) Initial (mg/L)	Biomass (g/L)	Time (min)	Max Sorption (mg/g)	Removal Efficiency (%)	Dominant mechanism	Unique feature/ Condition	Ref.
Chlamydomonas reinhardtii	12	1	180	4.65	38.6	Bioaccumulation & chelation	Wild type, moderate uptake	[53]
Chlorella vulgaris	12	1	180	3.89	32.4	Adsorption	Common green alga strain	
Scenedesmus almarinesis	12	1	180	5.00	41.7	Adsorption	Slightly higher uptake vs *C. vulgaris*	
Chlorella vulgaris	25	6	210	13.00	-	Adsorption	High biomass condition	[67]
Chlamydomonas sp.	200	0.6	60	53.8	95.2	Intracellular transformation	Highly tolerant to high-As	[56]
C. vulgaris + nano-ZVI	40	1.5	120	-	99.0	Hybrid (biosorption + Fe0)	Composite: Enhanced with NZVI	[57]
Nostoc NIES-2111_MUM004	0.1	-	-	-	39.72	Chelation & phosphate modulation	No phosphate added	[58]
Nostoc NIES-2111_MUM004	0.1	-	-	-	90.0	Chelation + enhanced uptake	With 0.24 mg phosphate	
C. sorokiniana MUM002	0.1	-	-	-	42.90	Chelation	Without phosphate	
C. sorokiniana MUM002	0.1	-	-	-	73.95	Chelation	With 0.24 mg phosphate	

Lead (Pb) Bioremediation

Lead (Pb) contamination remains a critical concern in aquatic environments due to its neurotoxicity, non-biodegradability, and tendency to accumulate in sediments and biota [20]. Microalgae have emerged as effective biosorbents for Pb^{2+} removal owing to the abundance of reactive functional groups on their cell walls—such as carboxyl, hydroxyl, amine, phosphate, and phenolic moieties which facilitate rapid and specific binding [29,68].

Pb^{2+} biosorption by microalgae is primarily governed by ion exchange and surface complexation. In these processes, Pb^{2+} displaces native cations such as Ca^{2+} and Mg^{2+} or forms stable PbOH-type complexes with hydroxyl groups at the cell surface [69,70]. Thermodynamic studies have consistently reported that Pb adsorption by microalgae is spontaneous and endothermic, highlighting the feasibility of using algal biomass under varying environmental conditions [71,54]. **Table 3** provides an overview of recent developments in Pb removal using various microalgae strains.

Kinetic analyses across multiple studies consistently align with pseudo-second-order models, indicating that chemisorption governs the rate-limiting step in Pb(II) biosorption by microalgae. Among green microalgae, *Scenedesmus sp.* and *Chlorella sp.* are frequently reported for their high uptake capacities, attributed to extensive surface area and dense functional groups. For instance, *Scenedesmus sp.* achieved a maximum Pb(II) binding of 102 mg/g with 85% removal efficiency under optimized conditions [72], while *Chlorella sp.* followed Langmuir adsorption behavior indicative of monolayer coverage [68].

Table 3 Recent advancements in Pb remediation by different microalgae strains.

Microalgae strains	Initial Pb conc. (mg/L)	Biomass conc. (g/L)	Time (min)	Max sorption (mg/g)	Removal efficiency (%)	Remark/ Mechanism	Ref.
Rhizoclonium hookeri	-	-	-	81.7	-	Spontaneous & endothermic; Sips isotherm fit	[73]
Phormium sp.	10	4	40	92.2	2.305	Dual Langmuir–Freundlich model; also for biodiesel use	[74]
Chlorella sp.	20	1.5	180	-	78	Langmuir isotherm; pseudo-second-order kinetics	[68]
Chaetoceros sp.	20	1.5	180	-	60	Freundlich model; multilayer binding	
Neochloris oleoabundans	10	-	5	-	93	Enhanced by DIC; rapid sorption; carboxyl & amide groups	[75]
Scendesmus sp.	100	1	60	102	85	Langmuir fit; pseudo-second-order; hydroxyl & amine groups	[72]
Spirulina maxima immobilized in alginate	100	1	360	87.9	-	Immobilized system; regenerable; electrostatic interactions	[76]

Beyond these species, several other microalgae and cyanobacteria also demonstrate promising Pb removal performance. *Neochloris oleoabundans* rapidly removed 93% of Pb within 5 min, aided by elevated dissolved inorganic carbon, which enhances the availability of carboxyl and amide groups for metal binding [75]. *Rhizoclonium hookeri* exhibited spontaneous, endothermic Pb sorption with high capacity (81.7 mg/g), fitting well with the Sips isotherm model [73]. Cyanobacteria such as *Phormidium sp.* achieved 92.2% removal within 40 min and showed dual Langmuir–Freundlich adsorption behavior, reflecting heterogeneous multilayer binding [74]. Diatoms like *Chaetoceros sp.* demonstrated lower efficiency (60%), with sorption best described by the Freundlich model [68].

Engineered systems have further enhanced Pb remediation efficiency. For example, *Spirulina plantesis* immobilized in alginate beads achieved 87.9 mg/g Pb uptake and maintained performance across multiple reuse cycles due to improved mechanical stability and resistance to metal toxicity [76]. Such immobilized biomass platforms are particularly useful for continuous-flow treatment systems where biomass retention and regeneration are critical. Given that Pb-saturated biomass can become a potential secondary pollutant if destabilized, recent reviews emphasize the need for post-treatment stabilization or recovery strategies. Techniques such as vitrification, hydrothermal carbonization to produce metal-enriched biochar, or controlled acid leaching for Pb recovery have been recommended to minimize metal desorption and reduce long-term environmental risks [39,77]. These steps are increasingly viewed as essential components in the development of safe, scalable, and circular-economy–aligned Pb bioremediation systems.

Mercury (Hg) bioremediation

Microalgae exhibit substantial potential for mercury (Hg) remediation through enzymatic and physicochemical mechanisms. One key pathway is the enzymatic reduction of Hg^{2+} to Hg^0, facilitated by mercuric reductase, followed by volatilization of elemental mercury. Additionally, intracellular processes may lead to the formation of insoluble compounds such as β-HgS (metacinnabar), mitigating Hg toxicity. These transformations reduce mercury's bioavailability and enable its removal from aquatic systems [18].

Recent developments in Hg bioremediation emphasize the optimization of uptake and resilience under metal stress through immobilization and bioengineering strategies (**Table 4**). For example, *Scenedesmus obtusus* XJ-15 demonstrated high uptake efficiency (95 mg/g) when cultivated in phosphate-enriched media, suggesting the critical role of phosphorus in functional group availability and metal binding [45]. Similarly, immobilized *Chlamydomonas reinhardtii* in Ca-alginate achieved 106.6 mg/g Hg^{2+} uptake, attributed to increased surface area and stability [78]. The integration of *Chlorella sp.* with a *Luffa cylindrica* support structure enabled 97% removal over 24 h while preserving cell viability under Hg exposure [79]. Other studies highlighted improved biosorption in strains such as *Pleurococcus* and *Concorcium* at low Hg concentrations, indicating their suitability for trace-level detoxification. Recent advancements in Hg remediation using microalgae have focused on enhancing adaptability, efficiency, and uptake through innovative cultivation and treatment methods (**Table 4**).

Immobilization strategies, such as modifying environmental conditions or using supportive matrices, have shown significant potential. For instance, *Scenedesmus obtusus* XJ-15 cultivated in a phosphate-rich medium exhibited a mercury uptake of 95 mg/g, emphasizing the role of functional groups as binding sites [45]. Similarly, immobilization of *Chlamydomonas reinhardtii* in calcium-alginate beads increased biosorption capacity to 106.6 mg/g, attributed to enhanced metal-binding sites [62]. Another approach utilized a *Luffa cylindrica* scourer to support living *Chlorella* sp., achieving 97% removal efficiency while maintaining cell viability under stress [80,81]. Both chemical and mechanical pretreatments have been employed to enhance the mercury-binding capacity of microalgae. Chemical modifications using acids, alkalis, or biopolymers alter surface functional groups and porosity, facilitating greater Hg(II) sorption. One notable approach is biomimetic mineralization, wherein a combination of polyelectrolytes and mineral coatings elevated Hg(II) uptake in *Chlorella vulgaris* from 62.85% to 94.74% [82]. Mechanical treatments, such as centrifugation and vacuum filtration, also contribute to improved removal by increasing contact efficiency and reducing biomass clumping. Interestingly, studies have shown that immobilized non-living biomass often exhibits higher removal efficiencies than live cells, particularly at high mercury loads. For instance, immobilized *Chlamydomonas reinhardtii* in Ca-alginate reached 106.6 mg/g Hg(II) uptake, benefiting from structural stability and resistance to Hg-induced toxicity [78,62]. Nevertheless, living biomass retains distinct advantages in continuous bioreactor systems due to its self-regenerating nature. This is evident in *Chlorella sp.* immobilized on *Luffa cylindrica*, which achieved 97% removal while maintaining cell viability over extended exposure [79,81]. These findings suggest that treatment selection should be tailored to system configuration, batch versus continuous and the anticipated Hg concentrations.

Table 4 Recent advancements in Hg remediation by different microalgae strains.

Microalgae strains	Initial Hg conc. (mg/L)	Biomass conc. (g/L)	Time (min)	Max sorption (mg/g)	Removal efficiency (%)	Remark/Mechanism	Ref.
Scendesmus obtusus XJ-15	20	0.125	180	-	-	Phosphate-enriched medium enhanced Hg binding	[45]
Chlamyomonas reinhardtii immobilized with Ca-alginate	500	-	-	106.6	-	Immobilized; improved stability and biosorption	[78]
Chlorella sp. (*Luffa cylindrica* support)	3	-	1440	-	96.47	Natural scaffold; maintains cell viability	[79]
Chlorella vulgaris	48	2	120	17.49	72.9	Surface sorption; conventional biomass	[83]
Scenedesmus sp.	0,007	-	20 days	-	64	Effective at low concentration; slow removal	[80]
Chlorella sp.	0,007	-	20 days	-	83	Trace Hg removal	
Pleurococcus sp.	0,007	-	20 days	-	86	Resilient in long exposure	
Concorcium	0,007	-	20 days	-	81	Community-based remediation system	
Chlorella vulgaris	100	-	90	35	70	Fast kinetics; moderate uptake	[81]
Chlorella vulgaris modified with biomimetic mineralization	0.01	-	5 days	-	94.74	Modified surface; enhanced trace-level Hg removal	[82]

Immobilization strategies, such as modifying environmental conditions or using supportive matrices, have shown significant potential. For instance, *Scenedesmus obtusus* XJ-15 cultivated in a phosphate-rich medium exhibited a mercury uptake of 95 mg/g, emphasizing the role of functional groups as binding sites [45]. Similarly, immobilization of *Chlamydomonas reinhardtii* in calcium-alginate beads increased biosorption capacity to 106.6 mg/g, attributed to enhanced metal-binding sites [62]. Another approach utilized a *Luffa cylindrica* scourer to support living *Chlorella* sp., achieving 97% removal efficiency while maintaining cell viability under stress [80,81]. Both chemical and mechanical pretreatments have been employed to enhance the mercury-binding capacity of microalgae. Chemical modifications using acids, alkalis, or biopolymers alter surface functional groups and porosity, facilitating greater Hg(II) sorption. One notable approach is biomimetic mineralization, wherein a combination of polyelectrolytes and mineral coatings elevated Hg(II) uptake in *Chlorella vulgaris* from 62.85% to 94.74% [82]. Mechanical treatments, such as centrifugation and vacuum filtration, also contribute to improved removal by increasing contact efficiency and reducing biomass clumping. Interestingly, studies have shown that immobilized non-living biomass often exhibits higher removal efficiencies than live cells, particularly at high mercury loads. For instance, immobilized *Chlamydomonas reinhardtii* in Ca-alginate reached 106.6 mg/g Hg(II) uptake, benefiting from structural stability and resistance to Hg-induced toxicity [78,62]. Nevertheless, living biomass retains distinct advantages in continuous bioreactor systems due to its self-regenerating nature. This is evident in *Chlorella sp.* immobilized on *Luffa cylindrica*, which achieved 97% removal while maintaining cell viability over extended exposure [79,81]. These findings suggest that treatment selection should be tailored to system configuration, batch versus continuous and the anticipated Hg concentrations.

From a sustainability and operational control perspective, immobilized microalgal systems and biofilm-based reactors are increasingly regarded as the preferred platforms for Hg remediation. These configurations minimize biomass washout, streamline the handling of metal-laden biomass, and enable stable operation in continuous-flow modes with comparatively low energy inputs for mixing and aeration [84]. Owing to the extreme toxicity and high bioaccumulation potential of methylmercury, recent assessments strongly discourage the use of open-pond systems. Instead, enclosed photobioreactors with stringent containment measures and dedicated post-treatment for both liquid and gaseous streams are recommended to prevent the release of volatile Hg species into the environment.

Cadmium (Cd) bioremediation

Microalgae exhibit diverse physiological and biochemical responses to cadmium (Cd^{2+}) exposure, including oxidative stress, lipid metabolism alterations, and activation of detoxification pathways. While Cd stress inhibits growth and chlorophyll biosynthesis in strains such as *Chlamydomonas moewusii*, *Arthronema africanum*, and *Coelastrella sp.*, it also induces adaptive mechanisms such as the upregulation of antioxidant enzymes (SOD, CAT, POD) and the biosynthesis of phytochelatins and glutathione [85-89]. In *Auxenochlorella protothecoides*, Cd exposure stimulates triacylglycerol accumulation and glutathione production, helping maintain lipid homeostasis under metal stress [87,88]. *Chlorella sorokiniana* responds by activating ROS-scavenging mechanisms and DNA repair pathways [89].

Recent strategies for Cd^{2+} removal have focused on selecting strains with high metal affinity and enhancing biomass recovery through self-flocculation. For instance, *Scenedesmus obliquus* AS-6-1 demonstrated 93.39% removal efficiency within 20 min, with high biosorption capacity (144.93 mg/g) under optimal pH and temperature [90]. Similarly, self-flocculating *Chlorella vulgaris* JSC-7 exhibited superior Cd tolerance and uptake due to phytohormone synthesis and unique cell wall characteristics compared to non-flocculating strains [91].

Genetic engineering has further improved Cd^{2+} resilience, as demonstrated by *Chlamydomonas reinhardtii* transformed with the *gshA* gene, which significantly enhanced glutathione synthesis and led to a 90.2% Cd removal within 6 h [92]. Bioimmobilization using alginate matrices also yielded promising outcomes. Immobilized *Turbinaria ornata* and *C. vulgaris* achieved up to 98.65% and 76.45% Cd removal, respectively, with higher sorption stability compared to free-living cells. Meanwhile, immobilization in polymer matrices such as sodium and calcium alginate has emerged as an effective alternative to improve stability, reusability, and tolerance under toxic conditions. *C. vulgaris* and *Turbinaria ornata* embedded in alginate beads achieved higher removal efficiency and greater biosorption capacity than free-living cells [91,93]. For example, immobilized *T. ornata* reached 98.65% Cd removal, likely due to enhanced surface area and ion exchange capacity [93]. In addition, *Chlorella sorokiniana* encapsulated in calcium alginate demonstrated 1.4-fold greater biomass yield and improved lipid productivity compared to non-immobilized cultures [94]. These physiological benefits suggest that immobilization may simultaneously support bioremediation and bioresource valorization. *Chlorella sp.* immobilized in 4% alginate beads maintained high cell density (1.07×10^6 cells/mL) over 15 d, with structural integrity retained for up to 21 d, indicating potential for prolonged operational use in wastewater systems [95]. Overall, the integration of genetic and physical enhancement techniques provides a promising avenue to improve Cd^{2+} remediation, with each approach offering unique benefits based on the system's operational needs and metal concentration levels. An overview of these advancements is summarized in **Table 5**.

Table 5 Recent advancements in Cd remediation by different microalgae strains.

Microalgae strains	Initial Cd conc. (mg/L)	Biomass conc. (g/L)	Time (min)	Max sorption (mg/g)	Removal efficiency (%)	Remark/ Mechanism	Ref.
Chlorella sp	10	1.5	-	15.51	92.5	Passive adsorption; free cells	[96]
Chlorella vulgaris	100	-	1,440	49	72	Endurance under prolonged exposure	[47]
Coelastrella sp.	100	-	1,440	65	82	Inhibited growth; oxidative stress response	
Scendesmus obliquus	100	-	1,440	25	46	Lower efficiency under standard conditions	
Parachlorella sp.	100	1	-	96.2	-	High biosorption capacity	[97]
Scendesmus obliquus AS-61	50	0.8	20	144.93	93.39	High performance in short duration	[93]
Chlorella vulgaris	75	1.6	30	-	99.35	Effective at short timeframes	[91]
Chlorella vulgaris immobilized with 4% Ca-alginate	75	0.025	30	-	76.45	Immobilized system	
Chlamydomonas reinhardtii wild type	1	-	360	-	90.2	Engineered with *gshA* for enhanced glutathione	[92]
Chlamydomonas reinhardtii PRO2	1	-	360	-	69.8	Control strain	
Suspended FACHB-12	3	-	120	60.03	61.8	Conventional setup	[98]
FACHN-12 biofilm with luffa sponge	3	-	120	78.76	72.5	Biofilm on natural support	

Microalgae strains	Initial Cd conc. (mg/L)	Biomass conc. (g/L)	Time (min)	Max sorption (mg/g)	Removal efficiency (%)	Remark/ Mechanism	Ref.
FACHN-12 biofilm with K3	3	-	120	133.14	92.7	Enhanced sorption + adhesion	
Didymogenes palatina XR	2	-	-	7.41	87.99	Trace-level treatment	[99]
Turbinaria ornata	26.19	4.96	-	23.9	94.34	Macroalga-based sorption	[93]
Turbinaria ornata immobilized with 4% Ca-alginate	25.2	5.04	-	29.6	98.65	Immobilized; high removal under batch conditions	

In recent studies, biofilm-based systems have emerged as effective platforms for cadmium (Cd^{2+}) removal. *Scenedesmus obliquus* (FACHB-12), cultivated on luffa sponge scaffolds, achieved a maximum Cd adsorption capacity of 133.14 mg/g, with a removal efficiency of 75.3% at an initial concentration of 3 mg/L [98]. This system benefits from enhanced biomass adhesion and surface area, improving metal uptake under controlled conditions. Similarly, *Didymogenes palatina* XR demonstrated 87.99% Cd removal at low concentrations, attributed to the formation of Cd-phosphate precipitates on the cell surface in high-phosphorus environments [99]. These studies underline the role of surface functionalization and nutrient modulation in optimizing microalgal Cd remediation. However, the temporal efficiency of Cd biosorption remains a concern. For instance, *S. obliquus* biofilms exhibited a decline in Cd removal efficiency shortly after the initial adsorption phase, suggesting potential saturation of active binding sites or desorption effects over time [98]. Moreover, competitive ion interference can hinder Cd uptake by *Chlamydomonas reinhardtii*, for example, preferentially absorbed Pb^{2+} over Cd^{2+} in mixed-metal environments, revealing selectivity limitations under real-world wastewater conditions. These findings indicate that while promising, microalgae-based Cd removal systems require further refinement. Future directions should focus on enhancing binding site specificity, engineering biofilms for sustained activity, and adjusting environmental parameters to overcome ion competition. A multi-metal remediation framework, incorporating selective uptake pathways and dynamic biosorption models, will be critical for advancing Cd^{2+} bioremediation in complex wastewater matrices.

Chromium (Cr) bioremediation

Among HMs, hexavalent chromium (Cr(VI)) is especially problematic due to its high solubility, oxidative potential, and carcinogenicity. Microalgae have emerged as sustainable tools for Cr(VI) remediation, leveraging multiple mechanisms that include extracellular adsorption, intracellular sequestration, and enzymatic reduction to Cr(III), a less toxic and less mobile form [46,100-102]. Extracellular polymeric substances (EPS) secreted by microalgae such as *Phaeodactylum tricornutum* and *Navicula pelliculosa* serve as effective biosorption matrices, rich in hydroxyl, carboxyl, and amino groups that bind Cr ions [103]. Beyond passive biosorption, intracellular processes, such as vacuolar sequestration and chelation by heat-stable peptides, contribute significantly to detoxification [87]. Importantly, chromate reductases enable microalgae to enzymatically reduce Cr(VI) to Cr(III) within the cytoplasm, further decreasing environmental risk [102,104].

Recent studies underscore the diversity of microalgae in Cr remediation capacities. For example, *Chlamydomonas moewusii* showed 90% Cr(VI) removal, while *Auxenochlorella pyrenoidosa* and *Scenedesmus sp.* achieved 80% and 65%, respectively, particularly useful in tannery wastewater contexts [104]. *Leptolyngbya boryana*, a cyanobacterium, demonstrated remarkable Cr(VI) tolerance up to 750 mg/L and 96.6% removal [105]. Notably, *Spirulina sp.* has been shown to adsorb both Cr(III) and Cr(VI), with potential dual roles in bioremediation and high-value pigment production [106]. Beyond mechanistic insights, the effectiveness of Cr(VI) bioremediation is highly dependent on strain-specific tolerance and accumulation capacity under variable environmental conditions. Multiple microalgal species have demonstrated promising performance even at elevated Cr(VI) concentrations, particularly those associated with tannery effluents. Optimization of cultivation conditions (light, nutrients, pH) and growth media formulations has been shown to significantly influence Cr uptake efficiency [105,106]. However, long-term exposure studies, metal competition scenarios, and real wastewater validations remain limited. The compiled data in **Table 6** illustrate the diversity and promise of microalgal strains in Cr remediation under varied operational settings.

Table 6 Recent advancements in Cr remediation by different microalgae strains.

HM Form	Microalgae strains	Initial Cr conc. (mg/L)	Biomass conc. (g/L)	Time (min)	Max sorption (mg/g)	Removal efficiency (%)	Remark/ Mechanism	Ref.
Cr(III)	*Chlorella vulgaris*	147	1	240	63.2	43	Moderate biosorption; applicable in mixed-metal settings	[107]
	Scenedesmus quadricauda biochar	10	2	240	-	100	Enhanced surface area via biochar promotes adsorption	[108]
	Scenedesmus quadricauda	100	2	120	-	98.3	Effective native strain; suitable for primary Cr(III) uptake	[109]
	Spirulina sp. NCIM5143 in Yamuna river	80	-	-	-	88.1	Field strain with strong Cr(III) tolerance	[106]
	Spirulina sp. NCIM5143 in Zarrouk medium	80	-	-	-	87	Good lab-scale performance with consistent media-based behavior	
Cr(VI)	*Spirulina platensis*	500	-	90	59.6	-	Efficient at high Cr(VI) concentrations; desorption effects present	[110]
	Chlamydomonas moewusii	-	-	-	-	90	High Cr(VI) tolerance and fast uptake; suitable for shock load environments	[104]
	Scenedesmus sp.	-	-	-	-	65	Moderate biosorption; potential for hybrid or co-remediation setups	

HM Form	Microalgae strains	Initial Cr conc. (mg/L)	Biomass conc. (g/L)	Time (min)	Max sorption (mg/g)	Removal efficiency (%)	Remark/ Mechanism	Ref.
	Auxenochlorella pyrenoidosa	-	-	-	-	80	Promising for Cr(VI) stress resilience and genetic enhancement	
	Leptolyngbya boryana	30	-	5 days	-	96.6	Exceptional long-term Cr(VI) tolerance in cyanobacteria	[105]
	Spirulina sp. NCIM5143 in Yamuna river	80	-	-	-	74	Lower Cr(VI) uptake compared to Cr(III); sensitive to ionic conditions	[106]
	Spirulina sp. NCIM5143 in Zarrouk medium	80	-	-	-	83.1	Stable Cr(VI) uptake; model for repeated lab applications	

Non-living microalgal biomass has gained attention as a promising biosorbent for both Cr(III) and Cr(VI) removal due to its chemical stability and reusability. Several pre-treatment strategies, such as methylation and chemical conditioning with NaOH or SDS, have been shown to significantly enhance the surface reactivity and metal-binding capacity of algal biomass. For instance, NaOH-treated immobilized biomass exhibited a desorption efficiency of 90.01% for Cr(VI) when used with chitosan carriers, suggesting its suitability for regenerable biosorption systems [111]. Similarly, Scenedesmus quadricauda, a chlorophyte microalga, demonstrated high adsorption potential for both Cr species in batch experiments. Chemical regeneration using NaOH successfully recovered 60% of the Cr(VI) sorption capacity, while HNO_3 restored 85% of the Cr(III) capacity [109]. These findings support the integration of chemical regeneration cycles in Cr bioremediation workflows, especially for large-scale operations. However, trade-offs exist between chemical efficiency and potential biomass degradation during repeated use, which highlights the need for optimizing pre-treatment dosage and frequency.

Multi-metal bioremediation

In real industrial and municipal effluents, heavy metals rarely occur in isolation; instead, Pb, Cd, Cu, Zn, Ni, Cr, and others are typically present as complex mixtures that compete for binding sites on microalgal cell walls and intracellular ligands [112]. Multi-metal systems introduce additional challenges compared to single-metal assays, including competitive adsorption, changes in speciation, and potential synergistic or antagonistic toxic effects on algal physiology. Recent experimental studies with green microalgae such as *Tetradesmus obliquus* have demonstrated that adsorption capacities and selectivity coefficients for individual metals can shift markedly when Cu^{2+} and Zn^{2+} are supplied together, underscoring the need to calibrate kinetic and isotherm models under mixed-metal conditions [113,114].

Early multi-metal biosorption work with macroalgae and microalgae (e.g., Sargassum and Chlorella) showed that affinity typically follows an order (Pb > Cu > Cd > Zn), with high-affinity metals suppressing uptake of lower-affinity ones when binding sites are limited [77]. More recent systematic studies confirm that microalgal cell surfaces provide a heterogeneous set of ligands (carboxyl, phosphate, amine, sulfhydryl), leading to metal-specific preferences that depend strongly on pH, ionic strength, and the presence of dissolved organic matter [115]. This complexity has motivated the development of multicomponent isotherm models and surface-complexation approaches to predict uptake in realistic wastewater matrices.

To address the limitations imposed by competition, several strategies have been proposed and, in some cases, tested: (i) mixed or consortial cultures, where combining microalgae and cyanobacteria with complementary metal preferences can broaden the overall removal spectrum; (ii) composite biosorbents, such as microalgae–biochar or microalgae–chitosan beads, which increase surface area and introduce additional functional groups while facilitating packed-bed operation; and (iii) amino acid– or polymer-assisted complexation, where small ligands (e.g., lysine) form ternary complexes with metal ions and algal surfaces, enhancing total uptake in both single- and mixed-metal systems [114,116].

On the cellular side, multi-metal exposure triggers broad stress responses that overlap with those induced by single metals. Comprehensive reviews note that microalgae adjust the expression of metal transporters, antioxidant enzymes, MTs, and PCs in a metal- and concentration-dependent manner, and that metabolic engineering aimed at increasing total thiol capacity or overexpressing specific transporters could, in principle, improve removal of several metals simultaneously [117,118]. However, multi-metal systems also raise important biosafety and ecological questions: Metal-laden biomass may contain a cocktail of toxic elements with differing mobility and bioavailability, and the release of engineered strains in open systems remains controversial. Consequently, recent reviews advocate for (i) using immobilized or enclosed photobioreactors for multi-metal remediation, (ii) coupling algal units with robust post-treatment (e.g., vitrification, pyrometallurgical recovery), and (iii) integrating techno-economic analysis and life-cycle assessment (LCA) to compare microalgal multi-metal remediation fairly with advanced physicochemical options [114,119].

Technologies to enhance microalgal bioremediation

Cultivation systems

Optimizing microalgal cultivation systems is central to enhancing HM bioremediation efficiency. These systems are designed not only to maximize biomass productivity but also to regulate critical parameters, such as pH, temperature, light intensity, salinity, and nutrient availability, that influence metal uptake and algal physiology [120]. Two primary cultivation configurations dominate the field: Open systems (e.g., raceway ponds) and closed systems, notably photobioreactors (PBRs). Each presents trade-offs in cost, control, and scalability [121,122].

Open ponds remain widely used because of their low capital and operational costs, simplicity, and suitability for large-volume wastewater streams. They are advantageous for treating municipal, agricultural, or aquaculture effluents, where high precision is not required. However, their susceptibility to contamination, evaporation, temperature fluctuations, and inconsistent irradiance often leads to variable metal-removal performance [123,124]. Moreover, dynamic physicochemical conditions in open ponds may alter HM speciation; for instance, pH shifts or dissolved organic matter fluctuations can reduce HM bioavailability, necessitating improved hydrodynamic design and real-time monitoring systems [125]. This variability was clearly demonstrated in a pilot study at a leather-processing facility in India, where *Chlorella vulgaris* isolated from the effluent exhibited substantially higher Pb adsorption under natural sunlight (30.6 mg g^{-1}) than under laboratory conditions (10.5 mg g^{-1}), and pilot-scale high-rate algal ponds achieved notable reductions of multiple metals through combined adsorption, complexation, entrapment, and possible phycovolatilization pathways [126]. These results highlight both the potential and environmental sensitivity of open-pond systems under real wastewater conditions.

In contrast, PBRs provide precise environmental control that enhances metal uptake rates and ensures culture stability. Tubular, airlift/bubble-column, and flat-panel PBRs allow optimized light distribution, gas exchange, and mixing, enabling high cell densities and consistent bioremediation performance even under fluctuating wastewater chemistries [120,127]. Their advantages are illustrated in a recent 30 L pilot system equipped with advanced microbubble aeration, where Chlorella vulgaris removed up to 95% of Cu, Cd, Ni, Pb, and Zn within only three days, underscoring the importance of efficient gas transfer and reactor control for accelerating metal-removal kinetics [128]. PBRs are particularly suited for high-strength industrial effluents (electroplating, mining, pharmaceuticals), where consistent redox conditions and CO_2/O_2 ratios improve Cr(VI) photoreduction and thiol-mediated sequestration. While operational costs are higher, PBRs enable year-round cultivation and predictable performance, an advantage for facilities with fluctuating HM loads. The integration of microalgal systems within wastewater infrastructure strengthens circular bioeconomy pathways, enabling nutrient recycling and biomass valorization into biofuels, feed, pigments, or biosorbents [122].

A major advancement in recent years is the emergence of immobilized and biofilm-based cultivation systems, which enhance scalability by improving biomass retention and simplifying solid–liquid separation. Immobilization matrices including calcium alginate, polyurethane foam, fibrous carriers, natural luffa scaffolds, and biochar–microalgae composites provide high surface-area-to-volume ratios, protect cells from metal toxicity, and enable operation under continuous-flow conditions [129]. These platforms are compatible with packed-bed, fluidized-bed, and membrane-integrated reactors, enhancing mass transfer, improving biosorbent reuse, and delivering stable performance under high metal loads [130]. Importantly, hybrid microalgae–bacteria consortia are increasingly recognized for their enhanced robustness and biosorption efficiency. When immobilized on porous carriers, these consortia form dense and synergistic biofilms that strengthen metal-binding capacity, improve tolerance to fluctuating wastewater chemistry, and offer superior operational stability compared to single-species systems. Evidence from multiple pilot studies shows that such hybrid configurations consistently exhibit higher metal-removal performance and greater resilience, positioning them as promising candidates for future industrial-scale operations [35].

Recent evaluations further demonstrate that well-designed microalgal systems can match or surpass conventional sorbents (activated carbon, ion-exchange resins) for multiple metals, while simultaneously providing circular co-benefits such as CO_2 capture, nutrient recovery, and biomass valorization [120,122,124]. Further progress has been driven by functionalized carriers, including metal-affinity beads, polymeric membranes, and nanomaterial-enhanced matrices (graphene oxide, Fe_3O_4 nanoparticles), which increase effective surface area, enhance selectivity, and simplify biomass handling, thereby improving efficiency in continuous-flow systems [129,130]. Together, these developments underscore the importance of system selection not only based on effluent characteristics but also on desired scalability, operational stability, and valorization pathways.

Scalability and industrial feasibility remain closely tied to energy demand, hydrodynamics, and harvesting efficiency. TEA consistently identify mixing, aeration, and harvesting as the dominant cost drivers. Enhancing economic feasibility typically involves using wastewater as culture media, deploying thin-layer or cascade reactors, developing self-flocculating or magnetically responsive strains, and integrating biomass valorization (biofuel, biofertilizer, pigments, biochar) to offset system costs [65,131]. Environmental sustainability evaluations via LCA show that microalgal–metal remediation can reduce GHG emissions by capturing CO_2, recycling nutrients, and minimizing chemical sludge formation. Nevertheless, electricity use in PBRs and the environmental burden of immobilization materials may offset these benefits, prompting movement toward renewable energy coupling, waste-heat recovery, and "wastewater-to-resource" biorefineries [65,132]. Digital innovations such as machine learning and IoT-based monitoring are increasingly integrated into modern operations. AI systems have been applied to optimize CO_2 dosing, light intensity, nutrient supply, and predict adsorption saturation kinetics, supporting real-time stability in industrial bioreactors [133,134]. These tools represent a critical future direction for scalable, automated, and energy-efficient microalgal remediation.

Genetic and metabolic engineering

The application of genetic and metabolic engineering has revolutionized the potential of microalgae as precision tools for HM bioremediation, particularly where native strains fall short in metal tolerance, uptake capacity, or stress resilience [135,136]. These bioengineering strategies address the limitations of conventional wastewater treatments—high cost, low selectivity, and secondary waste generation by tailoring microalgal traits for improved efficiency, selectivity, and sustainability [137,138].

Early genome-editing efforts primarily focused on *Chlamydomonas reinhardtii* due to its well-characterized genome [136]. However, advances in whole-genome sequencing, multi-omics, and synthetic biology have expanded the toolbox to include other taxa, broadening the landscape for tailored bioremediation platforms [138,139]. State-of-the-art editing tools, such as ZFNs, TALENs, CRISPR/Cas, and RNA interference (RNAi), allow precise modification of genes related to HM transport, redox homeostasis, and stress signaling [103,107,108]. Toolkits like Golden Gate MoClo and customized promoters have facilitated rapid engineering cycles, enabling strain-specific functional enhancements [139].

Protein engineering, which utilizes rational design, directed evolution, de novo design, and computational methods, enhances protein function or introduces new traits. For example, merging domains from different proteins can create fusion proteins with multifunctional properties, improved catalytic efficiency, and greater stability [129]. Machine learning accelerates this process by predicting the sequence-to-function relationships [140]. However, while these computational tools offer great promise, their predictive accuracy is often limited by the availability of well-annotated datasets, especially for non-model microalgal species.

Multi-omics data (genomic, transcriptomic, proteomic, metabolomic) continue to play a central role in identifying suitable engineering targets [48,141]. While powerful, integration across datasets is challenging, especially when moving from model organisms to extremophiles. Online platforms such as Phytozome and Algal Functional Annotation Tool facilitate cross-species analysis [48,142]. Environmental stress strongly influences the performance of engineered strains. Factors such as pH swings, fluctuating temperature, salinity, and redox instability can suppress engineered pathways. Consequently, ALE and environment-responsive promoter engineering are increasingly combined with genetic engineering to improve performance under industrially relevant stressors [43,62].

Genome-scale reconstruction and metabolic modeling have advanced microalgae as green cell factories but are still limited by incomplete annotation and underrepresented environmental interactions [143,144]. Meta-omics approaches have uncovered cooperative microbial interactions (e.g., *Chlorella*–bacteria consortia) that enhance nutrient removal and metal uptake [145,146]. Significant knowledge gaps remain in understanding how microalgae tolerate extreme metal loads, indicating an urgent need for deeper structural, cellular, and molecular studies. Expanding sequencing efforts and designing species-specific toolkits will be crucial for next-generation engineered strains [147].

Metal transporter as microalgal bioengineering target

Microalgae possess a diverse array of metal transporter genes, many of which are homologous to those found in higher organisms such as yeast, plants, and bacteria [148]. These transporters maintain intracellular metal homeostasis by regulating uptake, sequestration, and efflux across cellular membranes. In *C. reinhardtii*, these transporters are broadly classified into Group A—responsible for uptake and vacuolar sequestration—and Group B, which mediates efflux of excess metals from the cytosol. Transcriptomic studies have reported the upregulation of transporter families such as NRAMP, IRT, ZRT, ZIP, FTR, and CTR in response to heavy metal exposure [149]. Notably, the divalent metal transporter DMT1 plays a central role in mediating the influx of essential and toxic metals across the plasma membrane [150]. Functional studies have confirmed that overexpression of specific transporters, such as CrMTP4, can enhance cadmium tolerance and accumulation in *C. reinhardtii*, underlining the translational potential of transporter-based engineering for bioremediation [49].

In addition to classical metal transporters, sulfur metabolism contributes indirectly to metal tolerance through the generation of thiol-rich compounds that bind and detoxify heavy metals. ATP-binding cassette (ABC) transporters and Ca^{2+}/H^{+} antiporters have also been implicated in metal efflux and vacuolar compartmentalization [151]. Proteomic analysis in *Euglena gracilis* has further identified specific metal-binding proteins and membrane transporters involved in metal detoxification and accumulation [152]. Interestingly, horizontal integration of bacterial metal transporters into microalgae represents an emerging strategy. Transporters derived from *Escherichia coli*, *Ralstonia metallidurans*, and *Cupriavidus necator* have been explored to enhance uptake and compartmentalization of specific metals in photosynthetic hosts [153-155]. Collectively, the exploitation of metal transporters in microalgal systems represents a promising yet underdeveloped frontier. Future efforts should emphasize transporter specificity, kinetic modeling of uptake pathways, and subcellular targeting strategies to fine-tune metal acquisition and storage for optimized phycoremediation.

Metal chelation as microalgal bioengineering target

Metal chelation is a key intracellular strategy employed by microalgae to detoxify HM. Upon exposure to metal stress, microalgae upregulate the synthesis of thiol-rich organic molecules, which bind HM into stable chelate complexes, reducing their reactivity and oxidative potential [27]. These complexes are often sequestered in vacuoles or retained at the plasma membrane to prevent metal-induced cellular damage. Two main classes of metal-chelating molecules have received attention: MTs and PCs. MTs are cysteine-rich polypeptides involved in metal homeostasis and intracellular trafficking [156,157], while PCs are glutathione-derived peptides enzymatically synthesized upon HM exposure [27]. The biosynthetic pathway begins with γ-glutamyl cysteine and glycine, forming glutathione (GSH), which not only acts as an antioxidant but also serves as a precursor for PC production [40]. Experimental evidence suggests that increases in GSH and PC concentrations correlate strongly with improved tolerance to cadmium, mercury, and lead across diverse microalgal species [158].

Genetic engineering has further demonstrated the potential of enhancing chelation-based detoxification. Overexpression of PC synthase and GSH biosynthesis genes in microalgae such as *Chlamydomonas reinhardtii* significantly increases HM tolerance and accumulation capacity [92]. The targeted expression of these enzymes in specific organelles may further improve cellular resilience under high HM concentrations. Despite the known roles of MTs in higher plants, their functions in microalgae remain understudied. However, heterologous expression of plant-derived MTs in microalgae has shown promising improvements in metal sequestration capacity [159,160]. Proteomic analyses have also revealed stress-inducible metal-binding proteins that may complement the action of MTs and PCs in native microalgal strains [161,162]. These findings collectively underscore the need for a systematic exploration of chelation-related genes across microalgal taxa. Engineering strains with optimized MT/PC pathways, potentially coupled with transporter and antioxidant enhancements represents a synergistic strategy to improve metal sequestration efficiency for biotechnological and environmental applications.

Metal biotransformation as microalgal bioengineering target

Biotransformation represents a pivotal intracellular mechanism whereby microalgae convert toxic HM species into less harmful forms via enzymatic redox reactions. These transformations significantly lower the bioavailability and toxicity of metals, enhancing microalgal survival in contaminated environments [18].

A prominent example is the enzymatic reduction of hexavalent chromium (Cr(VI)) to trivalent chromium (Cr(III)) by chromate reductase (ChrR) in *Chlorella vulgaris*, facilitated by intracellular glutathione (GSH) [163]. This reaction diminishes Cr toxicity while aiding in its sequestration. Similar processes exist for other metals—arsenate can be reduced to arsenite, and mercury ions (Hg^{2+}) can be converted into elemental mercury (Hg^0), a volatile and less reactive form [164].

Recent advances in synthetic biology have demonstrated that transgenic expression of bacterial detoxification genes, such as mercuric reductase and membrane transporters (MerC, MerT, MerF, and MerP), enhances Hg^+ removal in *Chlorella* strains [165,166]. These genes mediate mercury uptake and reduction within the cytosol or across the chloroplast membrane, with chloroplast-targeting offering spatial containment but also raising concerns over photosynthetic efficiency. Researchers engineered microalgae containing bacterial genes to enhance HM detoxification. This includes the introduction of bacterial Hg reductase genes into *Chlorella* sp. [165]. Mercury detoxification involves inner membrane transporters (MerC, MerT, and MerF) that transport mercury into the cytosol, whereas the periplasmic guardian MerP ensures safe passage [166]. Beyond mercury, selenium detoxification involves enzymes such as selenocysteine methyltransferase (SMT), which convert toxic selenium into metabolically inert compounds. Other enzymatic systems, such as cytochrome P450s, contribute to tolerance by modifying metal-induced oxidative pathways [167]. Additionally, phosphate and ABCC transporters enhance arsenic and chromium detoxification through compartmentalization and efflux regulation. These enzymatic pathways reflect a diverse arsenal for heavy metal detoxification; however, many remain poorly characterized in microalgae compared to higher plants or bacteria. The photoreduction pathway in *C. vulgaris*, for instance, offers potential for solar-driven remediation, but mechanistic insights are still limited [168]

Oxidative stress regulation as microalgal bioengineering target

HM exposure induces the overproduction of reactive oxygen species (ROS) in microalgae, leading to oxidative damage of critical cellular components such as membranes, proteins, enzymes, and DNA. In *Chlamydomonas reinhardtii*, toxic concentrations of copper (Cu) significantly suppress growth, inhibit chlorophyll biosynthesis, and promote lipid peroxidation [169]. Similar oxidative responses have been reported under cadmium (Cd) and lead (Pb) stress in *Dunaliella salina* and *C. reinhardtii*, including the upregulation of genes encoding antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), glutathione-S-transferase (GST), peroxidases (POD, GPX), and glutathione peroxidase, which collectively detoxify ROS into less harmful forms [155,170,171]. In addition, heat shock proteins (HSPs) act as molecular chaperones, preserving protein functionality and preventing aggregation under HM-induced stress [172]. These responses not only mitigate ROS toxicity but also influence the overall resilience of microalgae under metal-contaminated conditions. Therefore, enhancing the biosynthesis of both enzymatic and non-enzymatic antioxidants through genetic engineering may represent a promising strategy to improve phycoremediation efficiency.

Metal stress response regulation as microalgal bioengineering target

HM stress in microalgae triggers intricate regulatory networks that include transcription factors (TFs), phytohormones, and microRNAs (miRNAs). These components orchestrate cellular responses that enhance microalgal tolerance and adaptability to metal toxicity. Transcription factors, such as metal response element-binding transcription factor-1 (MTF-1), regulate the expression of metal-detoxifying and antioxidant genes. Notably, TFs like RsMYB1 and WRKY13 have been shown to upregulate metal defense genes and strengthen antioxidant responses [173,174]. Phytohormones, including cytokinins (CKs), gibberellic acid (GA), and abscisic acid (ABA), modulate redox balance and enhance photosynthetic efficiency under metal-induced stress [175]. Genetic engineering has enabled the manipulation of these hormone pathways to create microalgal strains with superior stress resilience [176].

MicroRNAs (miRNAs) provide another layer of regulation by fine-tuning gene expression in response to metal stress. miRNAs such as miR395 and miR398 target genes involved in metal uptake, antioxidant activity, and hormone signaling, helping microalgae maintain cellular homeostasis [177-179]. Together, these regulators act in concert to elevate the metal tolerance of microalgae. Engineering these pathways offers significant promise for improving the phycoremediation potential of microalgal strains, enabling them to function not merely as passive survivors, but as precision tools in environmental detoxification.

Cell surface as microalgal bioengineering target

The cell surface of microalgae, particularly the cell wall, serves as a primary interface for HM interaction and plays a crucial role in initial metal binding and detoxification. Studies using cell wall-deficient mutants have confirmed the critical contribution of surface structures to metal tolerance and sequestration capacity [179,180]. To enhance these natural capabilities, researchers have turned to cell surface engineering, a strategy that involves the genetic modification of microalgae to express metal-binding proteins or peptides on the cell membrane. These engineered microalgae exhibit increased affinity for toxic metals through the external display of MTs and PCs, leading to improved biosorption efficiency [181,182]. For example, the surface expression of membrane-anchored MT polymers has significantly enhanced mercury (Hg) removal in aquatic systems [183]. Drawing inspiration from successful applications in yeast and bacteria, scientists have adopted surface display systems, including fusions with membrane proteins or anchoring domains to present synthetic peptides with high metal-binding affinity [184,185].

This approach offers multiple advantages. By localizing the metal-binding interface at the cell surface, it enables rapid uptake of metal ions before their entry into the cytoplasm, reducing intracellular toxicity. Furthermore, the strategy can be tailored for metal specificity, allowing selective adsorption and recovery of valuable elements such as gold, rare earth metals, and other industrially relevant ions. Importantly, by confining metal interaction to the extracellular domain, cell surface engineering mitigates the cytotoxic effects typically associated with heavy metal exposure. In addition to its technical efficacy, this approach aligns well with the goals of sustainable wastewater treatment by not only decreasing the environmental burden of heavy metals but also facilitating their recovery as resources. Thus, it exemplifies a convergence of synthetic biology, environmental remediation, and circular bioeconomy frameworks, positioning cell surface engineering as a promising platform for the advancement of next-generation phycoremediation technologies [130].

Roadmap for scaling genetically modified microalgae

To move genetically modified (GM) microalgae from laboratory concepts to real-world heavy metal bioremediation systems, we propose a staged scaling roadmap that explicitly integrates bioprocess development, regulatory approval, and biosafety management [136]. First, *strain qualification* is performed in closed laboratory photobioreactors, where engineered lines are characterized for genetic stability, metal removal performance across relevant effluent compositions, growth robustness, and potential for horizontal gene transfer. Second, *pilot-scale validation* is carried out in contained or enclosed reactors at industrial or municipal wastewater treatment facilities, under controlled access and monitoring. At this stage, process parameters (hydraulics, light regime, biomass harvesting) are optimized while tracking cell escape, changes in metal speciation, and long-term stability of engineered traits. Third, *pre-commercial deployment* involves scale-up to larger, modular GM-microalgae units integrated into existing treatment trains, supported by techno-economic assessment and life cycle analysis to confirm feasibility at operational scale [186].

Regulatory approval is embedded throughout this roadmap. Early in the strain qualification phase, environmental risk assessment, definition of realistic exposure scenarios, and evaluation of non-target effects are conducted in line with national GMO legislation and international biosafety frameworks (e.g., the Cartagena Protocol on Biosafety and its AHTEG risk-assessment roadmap, and the EU contained-use Directive 2009/41/EC) [187-189]. Ongoing efforts to mitigate biosafety concerns increasingly rely on layered containment, combining physical barriers (closed photobioreactors, immobilized or encapsulated biomass, membrane-separated reactors) with biological safeguards (auxotrophic strains, dependency on synthetic nutrients, inducible kill switches) that minimize the probability of long-term persistence or gene flow in receiving environments [190-193]. Proof-of-concept case studies with GM microalgae engineered for enhanced metal binding (e.g., overexpression of metallothioneins or phytochelatin synthase) and for wastewater polishing or CO_2 capture have already been demonstrated at pilot scale under regulated and contained conditions [27,117]. These examples provide a practical template for translating GM microalgae into heavy metal remediation applications by coupling a defined regulatory pathway with robust biosafety engineering.

Challenges and future perspectives

Despite the promising potential of microalgae for HM bioremediation in aquatic environments, several challenges hinder their full-scale implementation. One of the primary obstacles lies in the variability of environmental conditions. Factors such as light intensity, temperature, pH, and nutrient availability fluctuate widely in natural ecosystems, significantly affecting microalgal growth and metal uptake efficiency [194]. While advanced cultivation systems like closed photobioreactors offer precise control over these parameters, they come with elevated costs and increased technical complexity, limiting their application in low-resource settings [195,196]. In such contexts, affordable alternatives such as simple raceway ponds, high-rate algal ponds, shallow-depth paddlewheel channels, and low-tech PBRs constructed from transparent PVC tubes or repurposed plastic containers can provide a pragmatic compromise, ofering sufficient environmental control while keeping infrastructure costs low.

The intrinsic toxicity of heavy metals presents another challenge. While some species exhibit strong tolerance and uptake capacity, many others experience growth inhibition or cellular damage under high metal loads [9]. Genetic and metabolic engineering offer viable strategies to enhance the robustness of microalgae under such stress. However, the deployment of genetically modified microalgae in open aquatic systems raises critical ecological and regulatory questions. Biosafety, gene transfer risks, and environmental persistence of GMOs necessitate the establishment of comprehensive regulatory frameworks before large-scale implementation [183,194].

Scalability remains a formidable challenge. While laboratory and pilot-scale studies have demonstrated significant success, transitioning to full-scale applications requires substantial infrastructure and capital investment. The feasibility of such operations hinges on the development of low-cost, energy-efficient cultivation and harvesting technologies [26,29]. For microalgae-based systems to become commercially competitive, innovation in reactor design, biomass harvesting, and downstream processing is essential.

Looking forward, the integration of microalgal bioremediation into hybrid treatment trains offers a practical pathway to overcome some of the limitations of stand-alone systems. In wastewater treatment, microalgae can be coupled with conventional unit processes such as activated sludge, biofilm reactors, membrane bioreactors, constructed wetlands, and chemical precipitation steps to create synergistic configurations [28,197]. For example, algal–bacterial consortia in high-rate ponds or attached growth systems can simultaneously remove nutrients and heavy metals while reducing aeration demand, whereas microalgal polishing units placed downstream of primary or secondary treatment can target residual metals at low concentrations and improve effluent quality [198]. These hybrid systems are technically feasible within existing plant layouts, but their performance depends on careful control of hydraulic retention time, light availability, biomass harvesting strategies, and metal speciation. From an economic perspective, hybrid configurations can lower operating costs by decreasing energy use and chemical consumption, although they may require additional capital investment for photobioreactors, illumination, or harvesting equipment [199]. Therefore, site-specific techno-economic assessments and pilot-scale demonstrations are essential to identify the most cost-effective and scalable designs for municipal and industrial wastewater treatment. Furthermore, valorizing the post-treatment algal biomass into biofuels, animal feed, or agricultural biofertilizers can significantly improve the economic sustainability of these systems [26,200].

Future research must also address the molecular basis of heavy metal tolerance and uptake in microalgae. Understanding these mechanisms at the genomic, transcriptomic, and proteomic levels will support the rational design of more resilient and efficient strains. Interdisciplinary collaboration among microbiologists, environmental scientists, and bioengineers will be crucial in overcoming existing bottlenecks. Importantly, partnerships between academia, industry, and government will accelerate the translation of research into practical and scalable solutions for global water pollution challenges.

Conclusions

HM contamination in aquatic ecosystems remains a pressing environmental and public health concern, particularly because conventional remediation techniques are constrained by high operational costs, low efficiency at trace concentrations, and the risk of secondary pollution. In contrast, microalgae-based strategies offer a multifaceted solution that couples contaminant removal with environmental and economic co-benefits. Their inherent photosynthetic metabolism, tolerance to variable conditions, and capacity for extracellular biosorption, intracellular chelation, and enzymatic biotransformation position microalgae as promising agents for sustainable bioremediation.

This review has synthesized recent progress in microalgae-mediated HM removal, highlighting advances from strain selection and physiological optimization to genetic and metabolic engineering of transporters, chelators, and stress-response networks. Novel applications such as immobilized systems, biofilm-based reactors, and engineered photobioreactors have demonstrated improved process robustness and scalability. In parallel, multi-omics approaches and protein engineering have opened pathways to custom-engineered strains with enhanced remediation performance and metal specificity.

Looking ahead, several concrete directions for future research can accelerate the transition from laboratory studies to real-world deployment. These include (i) systematic optimization of microalgal strains for higher metal specificity, tolerance to mixed-metal and co-contaminant stress, and improved growth in non-sterile conditions; (ii) development of low-cost, resource-efficient cultivation and immobilization systems that can operate on non-arable land and use industrial or municipal wastewaters as growth media; and (iii) integrated techno-economic and life cycle assessments to identify cost drivers, optimize process configurations, and benchmark microalgae-based systems against conventional technologies. Further efforts are also needed to validate long-term performance under realistic effluent conditions and to understand how fluctuating pH, salinity, and organic loads influence metal uptake and regeneration of biosorbents.

From an implementation perspective, the industrial application of microalgae-based HM bioremediation will require coordinated action across academia, industry, and government. Strategic public–private partnerships and pilot-scale demonstration plants at mining sites, electroplating facilities, and wastewater treatment plants can help de-risk scale-up, refine operational guidelines, and generate performance data relevant for regulators and investors. Clear regulatory frameworks are needed to govern the use of native versus engineered microalgal strains, define discharge limits, and ensure safe handling and disposal or valorization of metal-laden biomass. Economic incentives such as green procurement policies, tax credits, and support for circular bioeconomy initiatives that valorize algal biomass into fuels, materials, and fertilizers can further enhance economic sustainability and encourage adoption, particularly in low- and middle-income countries where cost constraints are most severe.

By jointly advancing strain engineering, cost-effective cultivation technologies, rigorous techno-economic evaluation, and enabling policy frameworks, microalgae can progress from experimental tools to robust, field-deployable technologies for heavy metal bioremediation. Aligning these scientific and engineering advances with broader sustainability and regulatory agendas will be essential for the global implementation and long-term success of microalgae-based remediation systems.

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Declaration of Generative AI in Scientific Writing

AI-assisted tools were employed to streamline the language and improve the readability of the manuscript.

CRediT Author Statement

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Abbreviations

HM, heavy metal; SOD, superoxide dismutase; ASC, ascorbic acid; GSH, glutathione; ATP, adenosine triphosphate; ALE, adaptive laboratory evolution ; MMA, monomethylarsonic acid; DMA, dimethylarsinic acid; DCMD, direct contact membrane distillation; ROS, reactive oxygen species; TAG, triacylglycerol; AIE, aggregation-induced emission; PBR, photobioreactors; ZFNs, zinc finger nucleases; TALENs, transcription activator-like effector nucleases; CRISPR/Cas, clustered regularly interspaced short palindromic epeats/CRISPR-associated protein; RNAi, RNA interference; FBA, flux balance analysis; NRAMP, natural resistance-associated macrophage proteins; IRT, iron-regulated transporters; ZRT, zinc-regulated transporters; ZIP, Zrt-Irt-like proteins; FTR, Fe-transporters; CRS, chromium-resistant strain; CTR, Cu-transporter; DMT1, divalent metal transporter; GSH, glutathione; PCs, phytochelatins; MTs, metallothioneins; SMT, selenocysteine methyltransferase; GST, glutathione-S-transferase; GPX, guaiacol peroxidase; HSPs, heat shock proteins; TFs, transcription factors; miRNAs, microRNAs; MRE, metal response element, MTF-1, metal binding transcription factor-1; CKs, cytokinins; GA, gibberellic acid; ABA, abscisic acid; GM, genetically modified, PBR, photobioreactor; TEA, techno-economic assesment; LCA, life cycle assesment.

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