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A Review on Lead Toxicity and Its Mitigation

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KEYWORDS

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ABSTRACT: Various anthropogenic activities have resulted in major environmental concerns which includes residual hydrocarbons, heavy metals and various unessential trace elements. Lead is purely toxic in nature and its involvement in physiological or biochemical functions of the organism proved to be harmful. Its persistence in the environment and continuously increase in levels posing a serious threat in almost every country. Techniques such as phytoremediation, where the utilization of fungal and bacterial strains may help in reduction of the lead contamination areas proved to be better than conventional methods in aspects of safety and cost effectiveness. Plants, fungi, and bacteria are used to remove and degrade contaminants from soil and water. A wide variety of plant species have been used in phytoremediation research and practical applications. In the lab, some examples of bioremediation using fungi and bacteria have been tested. Microbial bioremediation can lower heavy metal concentrations because microorganisms, particularly bacteria, can sequester and transform them. Requirement of more efficient and potent means for the remediation of lead poisoning is obvious.

INTRODUCTION

Rapid expansion of industry and agriculture, as well as the disruption of natural ecosystems as a due to anthropogenic activities results in the leaching of heavy metals in the soil which poses a serious threat to our eco system [102]. Heavy metals contamination and its exposure to humans are due to anthropogenic activities and the utilisation of resources which are full of heavy metals [119]. Heavy metals and metalloids have been found in toxic levels in over 5 million different locations around the world [66]. Exposure to heavy metals pollution is posing a threat to the safety and quality of the agricultural and food supply chains [129]. Transition metals, metalloids, lanthanides, and actinides are heavy metals with metallic properties [107]. Cofactors may or may not be required depending on the enzyme [120]. The presence of trace amounts of impurities that binding proteins can detect can impair a cell's ability to function normally. Cobalt, copper, iron, manganese, molybdenum, and selenium are among the second group of trace elements [120]. Arsenic and cadmium like non-essential metals make their way through the cells and tissues just because of their physicochemical properties [25] [54]. This group is toxic to living organisms even at low levels of exposure, making it the most serious concern [9].

The most toxic metals to the environment, according to the EPA are lead, mercury, arsenic, cadmium, and thallium [35]. In the United States, the ATSDR only classifies all heavy metals as extremely toxic, including arsenic and mercury (Hg). According to the ATSDR's "top 20" list, most probable cause of heavy metal poisoning goes to arsenic, followed by lead and cadmium. The Earth's crust is rich in both non-metallic and metallic elements. Arsenic (As) is a poisonous substance. [85] [62]. Humans can be poisoned by both organic and inorganic forms of the element found in soil [115]. In flooded soils, because of their relative abundance there are more As^{3+} (arsenate) species than As^{5+} (oxyanions) species than in oxic environment [98] in response to this the

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inorganic As^{3+} species possess more toxicity and mobility than inorganic As^{5+} species [117] [55]. Complexes like hydroxides and iron (III) oxides reduce the mobility of As^{5+} on mineral surfaces [14] [36]. When groundwater iron levels fall, arsenic is easily converted to As^{3+}, according to the authors [36] [14] [11] [72]. Arsenate can be substituted for phosphate in biochemical reactions that use arsenate rather than arsenite [119].

Those who are exposed to lead-based pollution may experience a variety of health problems (Pb). Living organisms are affected by lead poisoning in a variety of ways. Lead, which accumulates in the top 8 inches of soil, has a wide range of morphological, physiological, and biochemical effects [137] [93] [121]. Soil iodine levels rise as a result of human activities such as mining, burning fossil fuels, and manufacturing [119]. In the absence of microbial consortia, the biogeochemical cycles and the remediation of heavy metal-contaminated environments becomes complicated [118]. Despite their toxicity, many microorganisms can tolerate and even thrive in their presence due to a variety of defence mechanisms [118]. Toxic metals are prevented from entering the cell by the plasma membrane and the cell wall (Resistance, Nodulation, Cell Division). Various sequestration techniques are used to keep metals out of cells. This method relies on metal ions accumulating outside the membrane in places like the periplasm or outer membrane, rather than metal ions complexing in the cell's interior to form insoluble compounds, as the other two methods do. Metal resistance is demonstrated by metallothionein and cysteine-rich proteins produced by *Pseudomonas* and *Synechococcus* species [99] [110].

Bacteria require biology and molecular biology in order to survive [74]. Metals are removed from the body by extrinsic metal ions through a variety of biochemical mechanisms [74] [128]. Heavy metal poisoning resistance genes can be found in both extrachromosomal elements and chromosomes. Heavy metal resistance is passed down through the generations on a molecular level [47]. To determine a person's tolerance to heavy metals, the MIC (Minimum Inhibitory Concentration) can be used (MIC). No microbes will grow if the MIC is less than the minimal inhibitory concentration [89]. For a long time, scientists have been researching microorganisms' tolerance to toxic metals, and this new study will be no different [79]. Soil heavy metal remediation is essential for environmental preservation and the protection of life-sustaining systems [38]. As a result, techniques like physical or chemical soil remediation may end up harming soil properties [108] [123]. In the bioremediation and phytoremediation methods, soil pollutants can be removed using microorganisms and plants [26] [1] [86]. For removing heavy metal contamination from a site, bioremediation is a cost-effective and environmentally friendly method [60]. Heavy metals can be extracted from insoluble ores using a variety of processes such as bioleaching and bio-oxidation. The use of biosorption and bio-oxidation in heavy metal remediation by microbes is critical [51]. Phytoremediation, on the other hand, is a long-term process that is heavily reliant on local environmental factors like weather, water, and soil [103] [21].

The interactions between plants, soil, and the atmosphere have an impact on environmental remediation. According to current research, phytoremediation of heavy metal-contaminated soil can be accomplished in four ways as reported [63]. Heavy metals can be removed from soil using microbial methods. Phytoremediation may be able to work in heavily metal-polluted environments because of plant-microbe interactions, according to new research [74]. Phosphate solubilization (indole-3-acetic acid production, cytokinins, gibberellins), siderophores, and the deamination of 1-aminocyclopropane-1-carboxylic acid are some of the mechanisms used by Plant Growth-Promoting Rhizobacteria (PGPR) [39] [27]. Improved metal mobilisation or immobilisation in biomass can be achieved through the use of PGPR on soils with heavy metal contamination [70] [74].

SOURCES OF LEAD CONTAMINATION

Solubility and mobility are the 2 prime factors which influences the toxicity of heavy metals [31]. Deep insights of physiochemical properties of lead eventually helps in the development of new innovative remediation technologies. Lead has no odour or colour change, unlike other metals. Despite its adaptability and flexibility, it is inefficient at delivering electricity [101]. Lead exists in a number of different oxidation states. In nature, the most common and stable forms of lead have been discovered [4]. Pb^{2+} produces mononuclear and polynuclear oxides and hydroxides. Metallic lead makes up the vast majority of lead found in nature. In the environment, copper, zinc, and silver all have a positive relationship with lead. Lead does not enter the soil or groundwater as a result of these processes. Precipitated lead is preferred over lead oxide because it is less flammable. When organic ligands like humic acid, folic acid, and EDTA react with inorganic compounds like Cl^-, PO_4^{3-}, CO_3^{2-}, SO_3, Pb $(OH)_2$, $(CO_3)^2$, $(SO_4)^2$, and Pb $(CO_3)^3$, they all adsorb on mineral surfaces, causing lead ions to precipitate in surface and groundwater [90] [138]. Amount of lead and its bioavailability over the surface or in ground water were greatly impacted by soluble salts, minerals, and pH. Anaerobic sediments are formed when tetra-methyl lead (an organic volatile) is alkylated according to [4] [75]. (Fig:1)

Lead contamination or pollution is caused by the presence of rich resources available in the Earth's crust. Basically, the anthropogenic activities were responsible for its major contamination. Only 0.0013

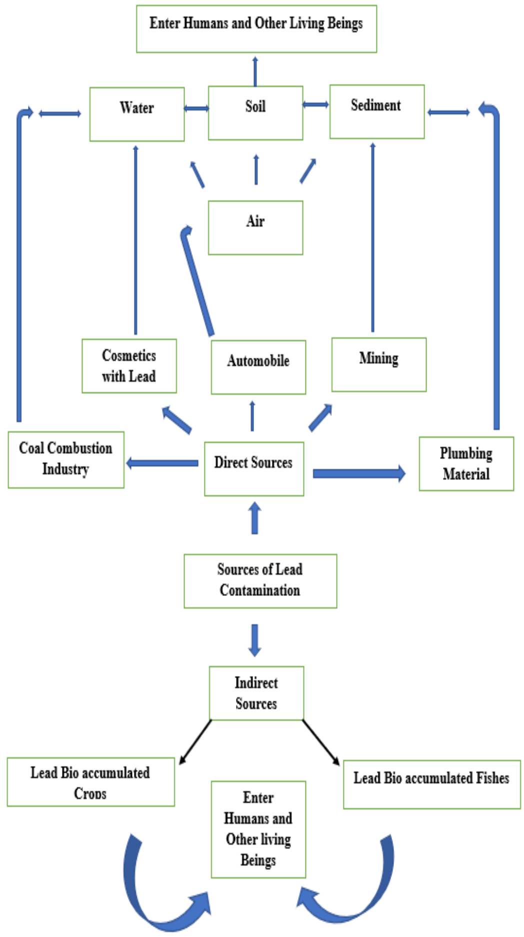

Figure. 1 Sources of lead contamination and their possible sites of accumulation

percent of the world's total supply of lead is currently available [88]. Most of the activities which leads to lead pollution and its exposure to humans are weathering of rocks, volcanic eruptions, industrial emissions, and the remobilization of resources which are highly rich in lead concentrations [113]. Soil erosion and runoff water in agricultural fields are the 2 most common ways for the leaching of lead into the environment [32]. Weathering has harmed the vast majority of lead that has been transported from its natural source [16]. Human activity is responsible for nearly all global lead pollution (98 %). According to a new study, lead pollution from historical metallurgy has been linked to human activity for more than two millennia. Lead contamination is heavily increased in

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the air since leaded gasoline became widely available in the 1920s [28]. Lead's low geochemical mobility can result in dangerously high levels in the environment [76]. Pb is a highly sought-after material in the manufacturing and processing industries for a variety of applications. Pb can be found in a variety of places, from batteries to paint pigments to metal plating and tin in metals like iron and steel. The widespread use of the metal in everyday items such as jewellery and toys, as well as traditional medicines and food, has exacerbated led pollution. The above-mentioned sources become the most common in recent times [91] [17]. As it is well known, lead-acid batteries are critical to the growth of the automotive industry. The utilisation of lead in the production of lead batteries holds almost 80% of the industrial value [18]. Despite the fact that lead battery recycling has begun, no concrete steps to reduce lead pollution have been taken [139]. Coal-fired power plants contribute significantly to lead pollution in the atmosphere through dust and aerosols [40]. Heavy metal contamination in topsoil is highest near smelters, and concentrations decrease as you go deeper into the soil. Metal is a musical subgenre distinguished by its heaviness and aggression [67]. Lead was widely used in the paint industry until 1978 because of its moisture-resistant properties. The lead content of paint has been reduced in many countries from 0.1-0.009 % [87]. (Fig: 2)

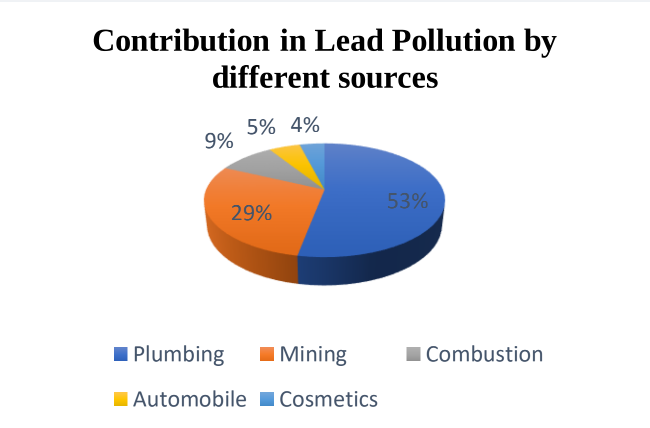

Figure. 2 Contribution in lead Pollution analysis of data (obtained from PubMed)

The use of certain cosmetics can result in lead poisoning [46]. In humans, acidic water is a major source of lead exposure. According to popular belief, acidic water is to blame for the corrosion of lead pipes and brass fixtures in water supply systems [87]. Water that has been exposed to lead-based plumbing contains a high level of lead. According to the World Health Organization, toxic metals such as lead can leach out of PVC pipes (WHO). Lead concentrations in the air are 1.5 times higher during Diwali fireworks, lead pollution is strongly linked to PM10 (particulate matter) [5]. Because of each of these industrial processes, there is lead pollution in the air. Only lead is a biodegradable substance in terms of persistence and even dispersal over long distances [78] [125]. Because of the dangers of lead exposure to humans, many people are concerned about lead pollution from household plumbing. If lead leaks from a home's plumbing fixtures, it can contaminate the water supply. Lead has a lower geochemical mobility in its natural state than lead in its synthetic form. Lead, a naturally occurring pollutant, is extremely rare. Lead pollution has increased because of human activity, contaminating water and soil.

EFFECTS OF LEAD CONTAMINATION

When lethal concentrations of heavy metals are present, they pose a threat to living communities. Even at the concentration of 10 mg/l lead has that potential to disrupt the endocrine system of sensitive organisms and at concentration of 1000 mg/l severe outcomes will be there due to its potency [17]. Lead makes its way through the food chain which make it highly toxic in nature covering every part of the ecosystem [124]. Even at low levels of contamination in the soil, plants can readily absorb lead. Humans and other living organisms consume lead through the edible parts of crops, which builds up in their bodies over time [114] [41]. Lead can enter the body through contaminated water, food, or dermal contact, as well as through placental transfer from the mother to the

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foetus or inhalation of polluted air [81] [52] [104]. The oxidative agent contained in lead causes oxidative stress when it enters a cell. Lead's toxic effects can be fatal because it is both teratogenic and mutagenic [76]. For lead exposure, the WHO recommends a weekly dose of 25 mg/kg. Lead exposure has been linked to encephalopathy, hepatitis, kidney failure, liver damage, anaemia, cancer, and neurodegenerative disorders, as well as gastrointestinal and cardiothoracic diseases and hearing loss in humans [81] [84] [52]. The teratogenic properties of lead can cause genetic abnormalities in an unborn child, which can result in miscarriage and infertility in women. Lead has been shown to inhibit the normal functioning of biomolecules such as DNA, proteins, and enzymes at the molecular level, posing a threat to the entire system [124] [111]. The long-term effects of lead on bone formation are well-known [124] [104]. Lead and other toxic metals has ability to accumulate in the bones for decades before being excreted or reabsorbed into the blood and organs. Adults only absorb 3–10% of the lead given to them orally, whereas children absorb 40–50%. [29] [84]. If blood lead levels in children under the age of six exceed 75 micrograms per litre, they are at risk of developing cognitive deficits [84]. If lead is not stored in the bones, it can be excreted through urine and faeces. Depending on the mode of lead exposure, the amount of lead excreted through hair and sweat varies. Children are more susceptible to lead poisoning as they don’t have a capacity to excrete it in comparison to adults [30] [77]. Plant growth and development have been harmed by elevated levels of lead in soil and water, which is an important part of the ecosystem. Cell damage is caused by a breakdown in the ionic balance within cells caused by oxidative stress induced by lead [57]. Physiochemical processes like cell division, production of chlorophyll, transpiration all are affected by the heavy concentrations of lead along which will have further effect on growth of seeds, their germination and overall development [61] [83]. Because lead accumulates in crops grown for human consumption, humans are exposed to it [114]. Soil quality is easier to maintain when there is a healthy microbial community to buffer the effects of outside influences. The composition of the microbial community changes because of exposure to various contaminants, including lead, whether direct or indirect. Lead contaminations has that potential which remarkably changes the functionality and phylogenetic properties of the microbial consortia. There is also a significant impact on the overall diversity of microbes in lead-contaminated areas [31] [67]. The microbial communities of various ecosystems are affected by lead pollution [58]. Lead has a negative impact on the microbial communities in soil as well as the soil's physicochemical properties. In addition to altering soil physicochemical properties, lead has a direct impact on soil nutrients. Lead poisoning is definitely a threat to upcoming generations if it’s not treated well. Lead poisoning is wreaking havoc on a variety of organisms in the ecosystem. Lead has a long-term effect on living things and the environment because it is non-degradable.

APPROACHES OF REMEDIATION

Scientists and experts from all over the world have been looking for long-term solutions to lead pollution. Despite extensive research, no long-term solution to lead pollution has been discovered. The major concern behind this is its long-term persistence in the environment [20]. Lead pollution can be reduced in a variety of ways, including through the implementation of environmentally friendly solutions. Chemical, physical, and biological methods are the most common methods for removing lead. Conventional methods which are used to treat lead contamination are electrochemical deposition systems, ion exchange, flotation, filtration, precipitation, sedimentation, and granulated activated carbon (GAC) adsorption [17]. But these methods will lead to secondary problems like low sensitivity, high cost, difficulty applying to large

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sites, and high energy consumption, to name a few drawbacks [109]. Environmentally friendly solutions will be required to eliminate lead pollution [23]. Microbial consortia have been used successfully for the remediation of wide range of pollutants as per the reports [115]. Bioremediation is the process of using living organisms to remove pollutants from the environment. Any living organism, including enzymes and exopolysaccharides, can help with bioremediation [23] [37]. Bacteria are widely regarded as the most effective bioremediation organisms due to their adaptability and versatility [12]. In recent years, the number of bacteria that can remove heavy metals like lead has increased. Bacteria showing resistance towards lead has been studied in wide range of organisms [140] [59].

PROCESSES

Bacteria, thanks to their adaptability and flexible metabolism, can be found almost anywhere on the planet. Numerous reports of bacteria that are resistant to lead have surfaced. In the presence of lead pollution, bacteria such as Acinetobacter sp. WQL9, Delftia, and Halomonas can thrive. Bacterial resistance to lead has been linked to several factors. We have developed a tolerance for lead because we've been exposed to it for such a long time [42]. Below are some examples of how bacteria have adapted to high-lead environments.

EFFLUX MECHANISM

An efflux mechanism is found in many lead-resistant bacteria. They break free from the cell and enter our environment, which can be hazardous. One of the most important modes of transportation [95]. Efflux mechanism has been employed by bacterial strains to remove lead from cells. Specialized cell membrane proteins found in effluent bacteria aid in the process. RND/CBA transporters, ability to resist, root nodulation, and cell division transporters are 3 major families of efflux proteins. The capsule biogenesis system is made up of three transmembrane pumps. In the capsule biogenesis assembly transporter, Gram-negative bacteria are commonly found. The Capsule Biogenesis Assembly Protein transports Ca^{2+} and other cations across the plasma membrane. Instead of cation diffusion transporters, cation diffusion facilitator transporters transport divalent metals from the cytoplasm to the periplasm. Cation diffusion facilitators play an important role in bacterial resistance when heavy metal concentrations are low [96]. ATPases (P-type ATPases) transport lead from the cytoplasm to the surrounding periplasm, in contrast to the chemiosmotic gradient. Metal ions such as copper, silver, and zinc are transported into and out of cells' mitochondria by sulfhydryl group-loving enzymes (adenosine triphosphatases). If an enzyme intermediate is involved in this reaction, it is referred to as a "P-type" reaction. P1B transporters are thought to play a role in cellular homeostasis and stress resistance (adenosine triphosphatases). The ability of a transporter to bind to metals determines its specificity (MBD). The adenosine triphosphatase P1B subfamily contains both intracellular and transmembrane segments (ATPases). ADP-dependent enzymes are divided into two types: P-type and CPx-type. Cysteine (C) follows or precedes conserved proline (P) in P-type enzymes (Adenosine Triphosphatases) (C). Efflux transporters keep the cell's metal ion homeostasis in order to prevent heavy metal poisoning, such as Pb poisoning [45] [42]. The p-type and CDF ATPases are the most common types of ATPases found in bacteria (adenosine triphosphatases). Efflux mechanisms are commonly used by bacteria to defend themselves against attack. Bacteria can perform lead bioremediation while maintaining a low lead concentration in their cells.

BIOSORPTION

The term "biosorption of lead" refers to the process by which lead adheres to the surface of bacterial cells. Biosorption is one of the most important mechanisms discovered yet in bacterial community which shows resistance to lead [10]. Because of their small size and rapid generation, bacteria are an effective biosorption agent. In the field of lead bioremediation, bacterial-

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mediated biosorption is a tried-and-true method. The rate of lead biosorption decreases as the binding sites become more crowded. Lead ions adsorb more slowly on the bacterial cell surface because of the repulsion of lead ions with similar charges. Various factors such as multiplication time, pH, initial lead concentration, and availability of bacterial strains have an effect on lead biosorption which eventually present shows it presence on the surface of bacterial cells [24]. The biosorption of lead reported by 2 bacterial strains Bacillus *pumilus* and *Bacillus cereus* increased significantly when the pH conditions has been enhanced from 1 to 6. Lead biosorption is most effective at a pH where bacteria have the most negative charge. Because H^+ ions compete with Pb ions for cell entrance at lower pH levels, lead absorption is more challenging [22]. As Enterobacter degrades proteins and amino acids, alkaline conditions for lead biosorption can be created [53].

Covalent bonds or ionic interactions can be used to apply lead to bacterial cell surfaces in one or more layers [73] [94]. Exopolysaccharides and cell wall-bound functional groups (such as hydroxyl groups) promotes the binding of lead to the cell surface of bacteria [49]. Biosorption mechanism helps in the regulation of lead transport across the cell membrane. The biosorption mechanisms of various bacteria and metals have been discovered by researchers. Lead bioremediation can benefit from the application of biosorption. Depending on the bacterial response, biosorption can be performed on either living or dead cells. On-site lead bioremediation is possible thanks to bacteria's ability to adsorb lead.

BIOPRECIPITATION

Precipitation or transformation with the help of microbial strains is very much promising which helps in reducing the lead toxicity. The activity of the enzyme phosphatase produces lead phosphate as a by-product [82] [100]. According to studies, it was reported that lead after precipitation can be accumulated on the surface or it can be expelled from the cell surface by bacteria. Because of their importance, phosphate-solvent bacteria (PSB) are essential for lead bioremediation [126]. Bacteria that break down insoluble phosphate compounds like Ca^3 produce the phosphate required for the lead bioprecipitation reaction $(PO_4)^2$. Insoluble lead-phosphate is formed when bioavailable phosphate reacts with no longer mobile lead [127]. Bacterial strains which convert soluble lead nitrate to insoluble lead phosphate will be determined as an anti-lead toxicity measure. In the bioprecipitation process, bacteria use the enzyme phosphatase to combine inorganic phosphate and lead ion [82]. Presence of lead extracellularly can be extracted from the cell walls of *Halomonas sp*. [2]. Lead precipitates and builds up on the membrane of Enterobacter species cells as a result of increased lead use [53]. PbS and lead are produced in anaerobic conditions, while lead oxide is produced in aerobic conditions (PbO). As a result of the presence of lead, which can cause dark precipitation to form. In order to prevent lead toxicity, enzymes are needed that break lead down into its elemental or other form. Due to the process preventing lead from entering bacteria, bio transformed lead is less toxic than lead that is not bio transformed [17]. *Halomonas sp*. produces lead nanoparticles when it aerobically denitrogenates Pb $(NO_3)^2$ [2]. Lead can be effectively removed from the environment using bacterial biotransformation and bioprecipitation mechanisms.

SEQUESTRATION

This process helps in the reduction of lead toxicity in the environment or cytoplasm, is one way. The body can absorb lead using both active and passive methods. Transporters deliver metal to cells during active absorption, while metal diffuses down to lower concentrations during passive absorption. Lead must be biosorbed into cells via a bacterial cell surface that is already present in the body. As a result, lead can still accumulate in the body [97] [6]. Transport from the nucleus to the vacuole or complexes with cytoplasmic molecules such as protein transport lead

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to the entry of cells. Heat shock proteins (HSP), metallothionein (MT), and glutathione transfer (GT) aid in the complexing of lead in Bacillus strains exposed to high levels of lead [6]. In vegetative cells of *Bacillus coagulans R11*, lead bioaccumulation is very much active than in decayed or spore forms. Under ideal conditions, these vegetative cells report removal up to 17.53 mg/g of lead. An active transport system responsible for the accumulation of lead instead of spores or dead bacteria [130]. In addition to but not limited to the foregoing, However, *Shewanella oneidensis*, a sulphate-reducing organism, aids lead bioaccumulation through diffusion. As lead bioaccumulation can have a variety of effects on bacterial bioaccumulation. Lead bioaccumulation is influenced by the growth phase and number of bacteria, as well as the concentration of lead, contact time, and pH. [7] came to the following conclusions. The initial high level of lead bioaccumulation in *Exiguobacterium profundum* is followed by a decline and then an increase as time passes [8]. According to [116] *Bacillus subtilis* has the greatest capacity to accumulate lead and does so at a later stage in the growth phase. As the amount of heavy metal in the environment increases, bacteria's ability to absorb lead decreases [7]. Despite the fact that lead removal at higher concentrations contradicts this phenomenon, there may be an unusual mechanism at work here, in which some dead cells with intact cell walls sacrifice themselves to allow living cells to deal with any residual low levels of lead [53], When bacteria accumulate lead, the toxicity of the substance is greatly reduced. The bioaccumulation mechanism can help with lead remediation. Future research could use bacteria that accumulate lead to remove lead from polluted areas.

SIDEROPHORE COMPLEXATION

These are low molecular weight compounds functions as ligand and possess strong affinity for Fe and act as chelator for Fe. These compounds are produced by plants when iron deficiency is there along with few microbes which also produces these compounds. Studies done by [43] has reported the production of siderophores by microbes when they are reeling under heavy metals stress condition. They possess several specific binding groups which helps in the binding with metals which simultaneously affects their affinity according to the type of metal being utilised. Release of these compounds from bacteria in presence of lead helps in the formation of complex which is not able to enter the cell, thereby helps in reducing the concentration of available free lead [43]. Various bacterial strains have been reported which are able to produce siderophores for the alleviation of lead contamination [122] [106] [135] [134] [68]. These compounds result in lead detoxification as well as in the promotion of phytoremediation processes [43]. Besides lead detoxification siderophores functions as protecting compounds which helps in the reduction of the concentration of free lead ions in surrounding environment. Hence it is necessary to have their secretion from microbial community which is required for proper functioning. *Bacillus megaterium sp.* has been reported to reduce the accumulation of lead in lettuce which indicates its potential application in the field of agriculture where lead contaminated sites are involved [126]. These compounds make lead immobilised by forming a complex, thus helps in the protection of human community form high levels of lead and facilitating its remediation.

An irreversible reaction took place after the uptake of lead where metallothionein's like proteins holds the responsibility for intracellular sequestration of lead [53]. It is clear now that mechanisms leading to remediation of lead are interconnected to each other and works in cohesion. Responses shown by individual bacteria comprising different mechanisms initiate various other responses in other microbial communities depending upon the elevated levels of lead and surroundings. Thus, we need to explore more molecular mechanisms of lead remediation which can help in designing innovative methods.

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PHYTOREMEDIATION APPROCHES

Lead toxicity has a negative impact on plant growth and phytoremediation. Metal is toxic to plants due to its wide range of solubilities. In the bioremediation of lead, plants and lead-resistant bacteria work well together. Plant growth has been shown to be aided by endophytic bacteria that are resistant to lead. When lead is present in the environment, they produce IDA (nitrogen fixation), which also aids in phosphate solubilization [15]. Plant growth-promoting microbes (PGPM) can be used to improve lead-contaminated soil [3]. Bacteria's ability to neutralise free radicals can help plants cope with oxidative stress. Metal-resistant, high-biomass plants that can cover a large area are required for bioremediation of a site. Plants can achieve all these characteristics thanks to symbiotic relationships with beneficial microbes. Accordingly microbial-assisted phytoremediation simplified lead bioremediation [3]. A microsymbiosis between *Robinia pseudoacacia* and *Mesorhizobium loti HZ76* can help with lead phytoremediation. Using materials that are resistant to lead. *Mesorhizobium loti HZ76* has a number of advantages, one of which is its ability to remove metals [34]. Plants use the bacterial enzyme aminocyclopropane-1-carboxylate deamine to make gasoline. Reduced ethylene production benefits stressed plants. The aminocyclopropane-1-carboxylate deaminase enzyme provides resistance to heavy metals. When *Acinetobacter sp*. Q2BJ2 and *Bacillus p*. Q2BG1 were introduced into contaminated areas, plant biomass and lead uptake both increased [136]. Bacteria produce indole-3-acetic acid, which suppresses primary root development while encouraging lateral and adventitious root growth [34]. Plants benefit from siderophore-producing bacteria because they increase iron availability [106] [134]. By binding to metals, siderophores have been shown to increase metal uptake in plants [136]. Bacillus sp. MN3-4 isolate produces indole-3-acetic acid and siderophore, both of which have been shown to aid plant growth. These strains can help to reduce toxic pollution [106]. Plant growth hormones, pseudomonas, and the siderophore produced by pseudomonas can all dissolve phosphate. These properties, as well as plant growth, can be used in lead bioremediation [71]. Bacillus subtilis has been shown to aid phytoremediation by assisting lead movement in the soil, even at extremely low temperatures. The use of these organisms in low-temperature bioremediation sites could be beneficial [19]. (Fig 3)

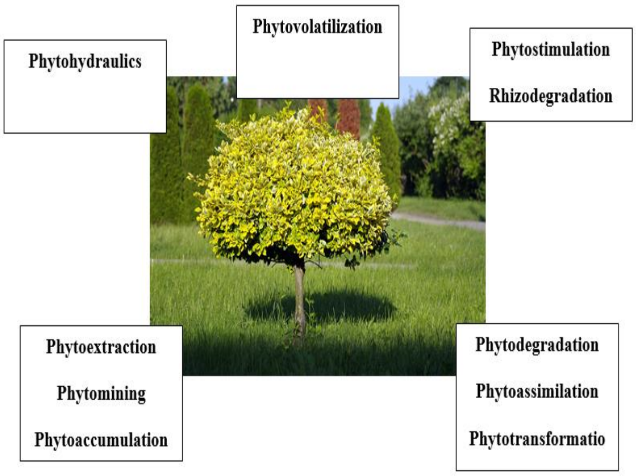

Figure 3. Phytoremediation techniques

When lead is bound to significant soil components, such as organic or inorganic matter, phytoremediation effectiveness is reduced. It may be as simple as introducing bacteria that are resistant to lead to solve this problem. The addition of bioaugmented, lead-resistant bacteria to the ground can improve plant uptake and solubility of lead. Some of the more common organic acids produced by bacteria include formic, tartaric, formic acid, and lactide (all of which are produced by bacteria). YSP40 and YSP151 are two microbes that help plants grow and remove lead-contaminated soil from the environment [133]. Bacteria and lead-resistant plants are mutually beneficial. Rhizoremediation employs the cooperation of plants and soil microbes to remove pollutants from the soil [50].

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Heavy metal/s	Source	Plant involved	Mechanism	Major findings	References
Cadmium	Industrial discharge, contaminated water and soil	Brassica juncea, Helianthus annuus	Accumulate Cd in their tissues through various mechanisms including ion uptake and sequestration	Indian mustard and sunflower are strong accumulators of Cd and effectively remove it from contaminated soil.	https://doi.org/10.1080/15226514.2022.2110036 https://doi.org/10.1016/j.envpol.2019.113085
Mercury	Natural deposits, coal-fired power plants, industrial processes	Eichhornia crassipes, Lemna spp.	Absorb and accumulate mercury from water through their root and shoot systems	High potential for removing Hg from aquatic systems	https://doi.org/10.1016/j.jhazmat.2010.11.009 https://doi.org/10.1007/s11356-022-22521-y
Lead	Old paint, contaminated soil, industrial emissions	Brassica juncea, Helianthus annuus	Can stabilize lead in the root system and reduce its mobility through root uptake and binding	Ability of these plants to accumulate and immobilize lead in contaminated soil	https://www.proquest.com/scholarly-journals/evaluation-sunflower-helianthus-annuus-l/docview/2206964807/se-2 ,

Table 1: Phytoremediation of Heavy Metals

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Arsenic	Naturally occurring in some regions, industrial processes	Ferns, Helianthus annuus	Accumulate As particularly in the roots via mechanisms such as uptake and translocation	Ability of certain ferns and sunflowers to accumulate and tolerate high levels of arsenic	https://doi.org/10.3390/plants9091211 https://doi.org/10.1007/s11738-023-03561-4
Chromium	Tanneries, electroplating, industrial discharges	Brassica juncea, Willow trees	Accumulate and reduce hexavalent chromium (Cr(VI)) to less toxic trivalent chromium (Cr(III))	Effectiveness of these plants in reducing chromium in contaminated soil	https://doi.org/10.1016/j.gene.2007.07.021 https://doi.org/10.1007/s10661-022-10625-4
Zinc	Industrial effluents, mining, agriculture	Thlapsi caerulescens, Willow trees	Hyperaccumulation, store Zn in their above-ground biomass	Potential in removal of Zn from contaminated soil	https://doi.org/10.1046/j.1365-3040.2000.00590.x https://doi.org/10.1080/15226514.2020.1773758

MOLECULAR RESPONSES TOWARDS LEAD

Wide variety of molecular mechanisms are exhibited by bacterial community which helps in dealing with the toxicity of lead. In response to the lead contamination some of the bacterial strains possess group of genes which get themselves activated in the presence of lead which makes these strains lead resistant promoting detoxifying mechanisms. [69] reported one of the lead resistant bacteria named as *Cupriavidus metallidurans* CH34 which contains a plasmid comprising of group of genes such as PbrT and PbrD which encodes for the uptake of lead and its binding which eventually helps in reducing lead toxicity. Along with the involvement of PbrT and PbrD, 2 more genes have been reported like PbrB/PbrC which helps in the production of membrane proteins and functions as signal peptidase and phosphatase. These membrane proteins help in the sequestration of lead after getting reacted with inorganic phosphate which is the by-product of by undecaprenyl pyrophosphate phosphatase. Same set of genes has been reported in *Achromobacter xylosoxidans* A8 [44]. The precipitation of lead is also linked with (ATP)-binding cassette (ABC) transporters which help in extracellular generation of

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phosphate. Lipoprotein LipA helps in the anchoring of lead to the outer cell membranes along with Na+/ H+ antiporter proteins which helps in remediation of lead upon exposure along with the uptake of protons from surroundings which promotes alkaline conditions. Further these conditions help in improving overall lead biosorption and precipitation [132]. Elevated levels of lead create oxidative stress in the surroundings and in lieu of this stress effect bacterial strains with heat-shock proteins like peroxiredoxin and thiol oxidoreductase needs to be explored which helps in the neutralization of this stress [68]. Along with these heat shock proteins, involvement of various other proteins and enzymes has also been reported which are involved in the transport of siderophores to the outer surfaces of membrane for detoxification utilising efflux mechanism [68]. Overall, we can say that remediation or detoxification of lead is a multi-facet approach rather that saying it a unified process where not a single bacterial strain is involved but the presence of consortia is highly considered along with the involvement of various detoxification mechanisms to overcome the toxicity created by lead.

Now we have the clear understanding of most of the bioremediation mechanisms that are able to define the things to certain extent. For example, in case of lead biosorption over the surface along with the accumulation intracellularly is possessed by lactic acid bacteria. Here we can define biosorption as physicochemical process, while accumulation comprises various other processes such as sequestration of metals inside cytoplasm, detoxification with the help of enzymes, and removal of lead by efflux process [65].

METALLOTHIONEIN

Because of their high cysteine content, low molecular weight metallothionein's prefer to bind heavy metals up to 30% [48]. Metallothionein provides protection to bacteria and various metabolic processes by immobilisation of non-essential or toxic heavy metals within the cell. Lead transport, storage, and detoxification, as well as intracellular sequestration, are all aided by metallothionein's. Heavy metal concentrations in the environment have a significant impact on bacterial metallothionein production. A bacterium that produces metallothionein, which can withstand high lead concentrations, is the best bioremediation tool. Presence of cysteine residues, metallothionein have that ability to bind up to seven atoms of lead in a single molecule [20]. Because metallothionein is required for the removal of lead from the body, it is a must [13]. Lead takes the top spot in active site metallothionein, according to simulations of both substances, where sulphur is found to weakly associate with lead. The relative positioning of cysteine residues is disrupted when lead binds to metallothionein's active site. Heavy metal hydration harms the stability of the metallothionein–metal complex which eventually effects the efficiency. Lead has a stronger affinity for metallothionein than any other heavy metal [92]. From water sources metallothionein, cellulose-binding modules, and super folder green fluorescent proteins were utilised for the remediation of lead. Metallothionein have played an important role in removing the toxic metal lead in this system [131]. Metallothionein can be produced by bacteria or extracted from bacteria for lead bioremediation. In the future, technology that can remove lead from polluted environments may be developed.

BOTTLENECKS AND CHALLANGES

The effectiveness of bioremediation can be influenced by a number of factors. Bioremediation of lead is heavily reliant on factors that affect bacteria's growth and metabolism. The use of bacteria for bioremediation has few limitations.

a. *Environmental conditions:* When it comes to heavy metals, the temperature is crucial. At extremely high temperatures, temperature-induced changes in cell membrane structure and bacterial growth reduce lead uptake [2]. The temperature-dependent fluidity of

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membranes has an impact on the membrane transport system. Changes in cell membrane composition caused by temperature slow lead biosorption on microbial cell surfaces. The deactivation of various proteins and enzymes at high temperatures has an impact on bacterial metabolism [80]. Temperature has its own effects on bioaccumulation of lead [105]. It's crucial to consider the temperature at which bacteria can thrive when using bacteria for lead bioremediation [64]. The removal of as much lead as possible is recommended, and pH is an important factor to consider [112]. By altering the surface charges of the cells, changing the pH of the medium affects how lead interacts with bacteria. According to theory, lead is more water-soluble at lower pH levels, making it easier for it to enter cells and disrupt metabolic processes than at higher pH levels [2]. As a result, pH has a significant impact on bacteria's ability to absorb lead. [80] and [66] conducted this research.

b. *Availability of nutrients:* Bacterial growth purely depends upon the type of nutrition they are getting. Lead can be removed from the body with the help of nutrients. Glucose aids in the absorption of lead in addition to serving as a carbon source. The electron-donor role of glucose aids absorption. Tryptone and other nitrogen sources, in contrast to yeast, increase bacterial resistance to lead. Bacteria require a variety of nutrients to absorb and detoxify lead [2].

c. *Other pollutants:* In addition to lead, polluted soil may contain other toxic substances. Bioremediation can be affected by the presence of additional toxic pollutants [53]. Bioremediation of lead is difficult when bacteria that are resistant to lead are also sensitive to other pollutants. A growing number of antibiotic-resistant bacteria are being discovered. Just to get the best, more bacterial strains need to be explored depending upon the type of waste being treated.

CONCLUSION

Lead is one of the most toxic toxins in the world. Given the recent rise in reports of lead pollution around the world, environmentally friendly lead remediation technology has never been more important. There are a wide variety of organisms that contain bacteria that are resistant to lead. Bacteria were the first to develop defences against lead poisoning. There was also an attempt to use lead-resistant bacteria in bioremediation techniques. Bioremediation has only a few real-world applications to date, according to our investigation: Biological bioremediation must begin immediately and continue for the shortest period of time possible. There is a need for more pilot-scale experiments because current research is limited to the laboratory. The best option for dealing with ground-level lead contamination may be local and multipollutant-resistant bacteria. The various lead remediation methods necessitate a better understanding of bacterial molecular responses. An understanding of the molecular interactions between bacteria and lead will help them remove lead from the environment more efficiently. Lead can be removed from the environment using bioremediation and immobilisation.

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