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Review

Lead Toxicity: Health Hazards, Influence on Food Chain, and Sustainable Remediation Approaches

Amit Kumar [1], Amit Kumar [2,*], Cabral-Pinto M.M.S. [3], Ashish K. Chaturvedi [4], Aftab A. Shabnam [2], Gangavarapu Subrahmanyam [2], Raju Mondal [5], Dipak Kumar Gupta [6], Sandeep K. Malyan [7], Smita S. Kumar [8], Shakeel A. Khan [9] and Krishna K. Yadav [10]

[1] School of Hydrology and Water Resources, Nanjing University of Information Science and Technology, Nanjing 210044, China; amitkdah@nuist.edu.cn
[2] Central Muga Eri Research and Training Institute, Central Silk Board, Jorhat, Assam 785000, India; aftab.csb@gov.in (A.A.S.); subrahmanyamg.csb@gov.in (G.S.)
[3] Geobiotec Research Centre, Department of Geosciences, University of Aveiro, 3810-193 Aveiro, Portugal; marinacp@ua.pt
[4] Water Management (Agriculture) Division, Centre for Water Resources Development and Management, Kozhikode, Kerala 673571, India; ashispc@cwrdm.org
[5] Central Sericultural Germplasm Resources Centre (CSGRC), Central Silk Board, Ministry of Textiles, Thally Road, Hosur, Tamil Nadu 635109, India; rmtarapur@gmail.com
[6] ICAR-Central Arid Zone Research Institute Regional Research Station Pali Marwar, Rajasthan 342003, India; deepak.gupta@icar.gov.in
[7] Institute of Soil, Water and Environmental Sciences, Agricultural Research Organization (ARO), The Volcani Center, Rishon LeZion 7505101, Israel; sanm@volcani.agri.gov.il
[8] Department of Environment science, J.C. Bose University of Science & Technology, YMCA, NH-2, Sector-6, Mathura Road, Faridabad, Haryana 121006, India; smita@jcboseust.ac.in
[9] Centre for Environment Science and Climate Resilient Agriculture, ICAR-Indian Agricultural Research Institute, New Delhi 110012, India; shakeel.khan@icar.gov.in
[10] Institute of Environment and Development Studies, Bundelkhand University, Kanpur Road, Jhansi 284128, India; envirokrishna@gmail.com
* Correspondence: amitkumar.csb@gov.in

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Abstract: Lead (Pb) toxicity has been a subject of interest for environmental scientists due to its toxic effect on plants, animals, and humans. An increase in several Pb related industrial activities and use of Pb containing products such as agrochemicals, oil and paint, mining, etc. can lead to Pb contamination in the environment and thereby, can enter the food chain. Being one of the most toxic heavy metals, Pb ingestion via the food chain has proven to be a potential health hazard for plants and humans. The current review aims to summarize the research updates on Pb toxicity and its effects on plants, soil, and human health. Relevant literature from the past 20 years encompassing comprehensive details on Pb toxicity has been considered with key issues such as i) Pb bioavailability in soil, ii) Pb biomagnification, and iii) Pb- remediation, which has been addressed in detail through physical, chemical, and biological lenses. In the review, among different Pb-remediation approaches, we have highlighted certain advanced approaches such as microbial assisted phytoremediation which could possibly minimize the Pb load from the resources in a sustainable manner and would be a viable option to ensure a safe food production system.

Keywords: lead toxicity; lead contamination; health hazards; remediation

1. Introduction

Lead (Pb) is a highly noxious, non-disintegrative heavy metal with a bluish-gray color, an atomic number of 82, molecular weight 207.2, density 11.34 g/cm^3, and a melting point of 621.43 °F. It can be easily shaped, molded, and used to form alloys through mixing with other metals. It can exist in both organic as well as inorganic form. The inorganic Pb dominantly occurs in dust, soil, old paint, and other different user products, while organic Pb (Tetra-ethyl Pb) is predominantly found in leaded gasoline. Both of these forms of Pb are toxic, however organic Pb-complexes are excessively toxic to biological systems compared to inorganic Pb [1]. Pb is the second most toxic metal after Arsenic (As), comprises 0.002% of Earth's crust [2,3], and its natural level remains to be below 50 mg kg^{-1} [4]. Although earlier literature did not focus on the biological importance of Pb, recent findings suggest that traces of Pb (~29 ng/g diet) is important for enzyme activities and cellular systems, especially during cell development, hematopoiesis, and reproduction [5].

In general, Pb salts/oxides through atmospheric dust, automobile exhaust, paint, polluted food, and water are the key pathways for human exposure. The food canning industry is also an important source of Pb intake due to its leaching ability into canned foods. Currently, humans are exposed to Pb through dust particles from soil transmitted into homes and/or drinking water. Lead is considered carcinogenic (Group 2B) to humans [6]. Humans are impacted by Pb primarily through ingestion as 20–70% of ingested Pb is absorbed by the human body. Children have a high absorption capacity of Pb [7,8].

Enhanced Pb concentration in blood affects behavior, cognitive performance, postnatal growth, delays puberty, and reduces hearing capacity in infants and children. In adults, Pb causes cardiovascular, central nervous system, kidney, and fertility problems. During pregnancy, Pb can also hamper fetal growth in the early stage [1,3]. The Commission Regulation E.C., No 1881/2006, documented the Pb concentration (0.3 mg kg^{-1}) thresholds for different agriculture products such as leafy vegetables and fresh aromatic herbs [9]. Pb sources, their inclusion in soil, Pb bioavilability to plants, soil role for Pb transfer to plants, plant toxicity and accumulation mechanism, Pb effect on plants and humans, and different remediation technologies are basically covered in the present review. The main objective of this review is to summarise the research updates on Pb toxicity, bioavailability, and its imposed toxic effects on plants and on human health, including recently tested/recommended remediation options.

2. Methodological Approach for Selecting and Reviewing the Literature in a Meaningful Way for Targeting Specific Objectives

2.1. Collection, Compilation, and Identification of Relevant Literature for the Study

The criteria for selection of recent literature for targeting up-to-date information on the topic was done through search string/keywords such as "Lead", "sources of Lead", "Lead toxicity", "bioaccumulation of Pb in food and human", "toxic forms of Pb", "Pb tolerance in human and plants", "health effect of Pb toxicity", and "Pb remediation". The extensive search of existing literature on the specific keywords was performed to collect the data from Scopus, Science Direct and Google scholar, MDPI, and other academic university websites. Three important criteria were considered for addressing relevant updated information (i) peer-reviewed, (ii) highly cited (i–10), and (iii) articles appearing in journals with a minimum impact factor (>1.0, *Thomson Reuters*) (iv) few articles except the above listed criteria based on recent/specific information was also included. The selection criteria/rules were adopted and modified from Sandin and Peters [10].

2.2. Extraction of Data and Data Representation

All the available relevant literature was studied carefully based on the key objectives of the present review. Omission of work was based on literature that was published before 2000, was without quantitative results, non-English, and/or was general/duplicate/similar in nature, which did not fit the questions of this review. Later, the results from all representative literature published from the year 2000 onwards were extracted and represented in tabular form.

3. Sources of Pb Contamination in Soil, Crops, and Water Resources

Pb contamination in air, soil, and water resources has been associated with natural causes, such as geochemical weathering, sea spray emissions, volcanic activity, and remobilization of sediment, soil, and water from mining areas [11–13]. Table 1 represents the various sources of lead contamination in agricultural soils, crops, and water in different countries/regions of the world. It is evidenced in Table 1 that the anthropogenic products and processes (such as industrial, oil-processing activities, agrochemicals, paint, smelting, mining, refining, informal recycling of lead, cosmetics, peeling window and door frames, jewelry, toys, ceramics, pottery, plumbing materials and alloys, water from old pipes, vinyl mini-blinds, stained glass, lead-glazed dishes, firearms with lead bullets, batteries, radiators for cars and trucks, and some colors of ink) are considered to be major sources of Pb contamination in the environment [14–21].

Pb is available in soil/sediments as a free metal ion, is associated with inorganic molecules (e.g., HCO_3^-, CO_3^{2-}, $SO_4^{\ 2-}$, and Cl^-), and can also exist as organic ligands (e.g., amino acid, fulvic acid, and humic acid). Pb can also be adsorbed onto particle surfaces such as biological material, oxides of iron, clay particles, and organic matter [22,23]. In general, a higher concentration of anthropogenic Pb accumulates on the soil surface and can decrease with depth [24]. Pb has a high affinity with organic and colloidal materials and, thereby, is readily available for plant uptake [25].

Table 1. Table of Pb contamination in agricultural soils, crops, and water in different countries [18].

Sources	Contaminati-on	Plant Species	Region	References
Wastewater of Shitalakhya river	Soil and vegetables	*Amaranthus lividus*, *Basella alba*, *Cucurbita moschata*, *Spinacia oleracea*, and *Trichosanthes cucumerina*	Bangladesh	[26]
Wastewater treatment plant	Soil, water, and crops	*Eruca sativa*, *Madia sativa*, *Malus sylvestris*, *Triticum æstivum*, *Triticum turgidum*, *Urtica dioica*, and *Vicia faba*	Morocco	[27]
Mine affected area	Soil and vegetable	*Amaranthus dubius*, *Ipomoea aquatic*, *Ipomoea batatas*, *Phaseolus vulgaris*, *Piper nigrum*, *Solanum lycopersicum*, and *Solanum melongena*	China	[28]
Sewage water	Soil and crop	*Oryza sativa*	Iran	[29]
Agricultural/Urbanisation activities	Water and sediments	*Lemna minor*	India	[30]
Urbanization	Soil, water, and vegetables	*Brassica oleracea*, *Momordica charantia*, *Phaseolus vulgaris*, *Raphanus raphanistrum*, *Solanum lycopersicum*, and *Triticum aestivum*	China	[31]
Anthropogenic activities	Soil and vegetables	*Cucurbita maxima*, *Lagenaria siceraria*, *Solanum melongena*, and *Spinacia oleracea*	Pakistan	[32]
Glass industry	Soil and agricultural crops	*Brassica juncea*, *Hordeum vulgare*, and *Triticum aestivum*	India	[33]

4. Pb Bioavailability in Soil and Its Influencing Factors

Lead bioavailability in soil is strongly controlled by its species, especially free-Pb ions concentration [22,34]. Plants absorb lead in dissolved form via the soil solution [25]. Moreover, the concentration of the free lead ion in soils depends on its physical process (e.g., adsorption/desorption) [23].

The behavior of lead species (bioavailability, mobility, and solubility) in soil is controlled by complex interactions of different biogeochemical factors [25]. These factors are redox conditions [35], pH [23,36], cation-exchange capacity [23], soil mineralogy, biological and microbial conditions [2], lead quantity [26,37,38], inorganic and organic legend concentration [22,34,39], competing cation concentration [40,41], and the type of plant species involved [37]. The behavior (uptake rate) of lead species in soil and plants is influenced by either biogeochemical factor independently or in combination with geochemical factors. The effects of some factors on Pb bioavailability are summarized below:

4.1. Soil pH

Soil pH is the most important factor that controls Pb availability to plants. Soil pH dictates Pb availability in soil as a negative correlation between Pb solubility and soil pH is noticed [42]. In acidic soil ($pH < 7$), Pb exists as aqueous $Pb(H_2O_6)^{+2}$, while in alkaline soil ($pH > 7$), Pb forms aqueous complexes with OH^- (hydroxyl ions). Specific adsorption of Pb is directly proportional to soil pH [16,43]. At a low soil pH (3–5), adsorption is the dominant process, whereas at a high pH (6–7), precipitation is the dominant process [16,44].

4.2. Soil Redox Potential

Redox potential controls Pb dynamics in soil. The solubility of Pb is inversely proportional to soil redox potential (i.e., Pb solubility increases along with a decrease in soil redox potential). Generally, heavy metals dissolve easily in waterlogged soils. Pb was dissolved by acetic acid in highly impeded drainage soil (1.9 $\mu g\ g^{-1}$) as compared to freely drained soils (0.1 $\mu g\ g^{-1}$) in a region of slate bedrock [16].

4.3. Soil Texture

Soil texture significantly affects Pb solubility. In Clay soils, heavy metal ions are adsorbed through ion exchange and specific adsorption mechanisms [45]. Pb adsorption also varies between types of clay minerals [16]. For example, the affinity between iolite and Pb is ~32 times higher than montmorillonite [46]. Mao et al. [47] observed low Pb adsorption on montmorillonite due to competition between Ca and Pb for cation exchange sites on clay.

4.4. Soil Minerals

Soil minerals such as Mn and Fe affect Pb solubility in soils. Mn oxides have a high affinity towards Pb, thus they significantly decrease Pb uptake by plants grown in Pb contaminated soil [2,16,48–50]. O'Reilly and Hochella [50] emphasized that microbial activity is responsible for Pb mobilization from oxides and carbonate. Tao et al. [51] reported that earthworms could enhance Pb availability to plants.

4.5. Nutrients, Organic Carbon, and O_2

These are the essential factors for microbial growth and metabolism and are directly involved in the degradation of contaminants. Some of the bioactive nutritional elements include carbon (e.g., backbone of all organic compounds), nitrogen (e.g., cellular protein and cell wall component synthesis), phosphorus (e.g., cell membrane, ATP, and nucleic acid), sulfur (e.g., amino acid synthesis), calcium (signaling transport), and magnesium (e.g., enzymatic activities functioning) [52,53] etc. Zhao et al. [54] concluded that soil physical properties such as permeability and fracturing could also affect Pb dynamics in soils. Li et al. [48] elucidated the effect of soil organic matter (OM) on Pb solubility through the formation of complexes during metals' interaction. Kögel-Knabner et al. [49] emphasized that soil OM drives a sizeable amount of Pb concentration by the formation of organo-Pb complexes.

The ion exchange capacity (particularly CEC), pH, ion redox potential, microbial community, texture, mineralogy, and organic matter of soils are the key regulating factors that affect Pb dynamics (e.g., adsorption, solubility, and mobility) in soil and bioavailability to plants.

5. Lead Bioavailability/Bioaccessibility in Animals and Humans

Lead toxicity is an important environmental health hazard and its effects on the human body are devastating. Total Pb in a human body is subject to environment, age, and occupation. It is estimated that a person weighing 70 kg will have an average of 120 mg of Pb, with 0.2 mg/L in the blood, 5–50 in their bones (in mg/kg), and 0.2–3 in tissues [55]. The Center for Disease Control and Prevention (USA) has set the standard elevated blood Pb levels for both adults and children (10 μg/dL and5 μg/dL, respectively) [56].

Bioavailability (BA) is an ingested fraction that crosses the gastrointestinal epithelium and is distributed into internal tissues and organs [57]. Bioavailability of Pb was established through in-vivo models such as in mice (*Mus*), monkeys (*Cercopithecidae*), rabbits (*Oryctolagus cuniculus*), rats (*Rattus*), and swine (*Sus scrofa*). However, extrapolation of the in-vivo models into human has not provided a realistic effect due to their physiological differences and species diversity. In-vivo experiments are much simpler than epidemiological studies because they are cheaper, faster, highly reproducible, and do not involve ethical issues. However, critical parameters (e.g., exposure levels, conditions, and absorbed Pb concentration) need to be considered while performing *in-vivo* specimen evaluation. The following key factors are to be considered for decision making in public health issues using in-vivo models: (a) specific features and limitations of the model; (b) targeting the human population in the design of animal studies at developmental stage; (c) the use of acceptable environmental doses, and (d) Pb speciation. In-vitro studies such as Relative Bioavailability Leaching Procedure (RBALP), Unified Bio-accessibility Research Group Europe Method (UBM), Solubility Bio-accessibility Research Consortium assay (SBRC), Physiologically Based Extraction Test (PBET), In Vitro Gastrointestinal (IVG) Method, and the In Vitro Digestion Model (RIVM) can be used to measure Pb bioaccessibility [58]. Pb relative bioavailability (RBA) refers to the comparative bioavailability of different Pb forms that are available in source substance [58]. For estimating the relative bioavailability of Pb, a reference material such as Pb acetate can be used. Lead RBA in soil can be measured by either blood or tissues (kidney, liver, and femur) [58,59]. Deshommes et al. [60] conducted an in-vivo experiment on Pb particles (especially particulate Pb forms including those in paint and dust and those in drinking water supply systems) and stated that the relative bio-accessibility leaching procedure (RBLP) offers the highest degree of validation and simplicity in animal models.

Literature suggests that due to unavailability of data and the existing model (e.g., animal model), we could not predict/estimate human risk assessment and human absorption of Pb particles, particularly for childhood exposure assessment, e.g., neuro-behavioral and neuro-developmental deficiencies, and the effects on growth, hearing, and blood pressure.

6. Lead Transportation, Toxicity, and Bioaccumulation Through Food Chain Contamination

Lead is one of the most toxic and frequently encountered heavy metals in the environment [34]. Different quantitative indices are currently being used to estimate Pb toxicity at trophic levels in the food chain (Table 2). Once Pb reaches the soil by any source and penetrates into the plant root system, it may accumulate there or may be translocated to aerial plant parts (APP). Pb mostly accumulates (≥95%) in the roots of plant species and only a small fraction is translocated to APP. Some of the studied plants species with respect to Pb transportation, toxicity, and bioaccumulation are *Allium sativum* [61], *Avicennia marina* [62], *Pisumsativum*, *Phaseolus vulgaris* and *Vicia faba* [34,63,64], *Lathyrus sativus* [65], *Nicotiana tabacum* [66], *Sedum alfredii* [67], *V. unguiculata* [68], and *Zea mays* [69].

Generally, plants uptake metal ions from soils through their roots [17,18,20]. Pb from the soil solution is adsorbed (unevenly) through roots and is bound with the uronic acid/polysaccharide of rhizoderm in many plant species such as *Brassica juncea* [70], *Festuca rubra* [71], *Funaria hygrometrica* [72,73], *Lactuca sativa* [74], and *Vigna unguiculata* [68]. This adsorbed Pb passively enters in roots and is transported through xylem. A concentration gradient was observed near the root apex, except for root cap, where cells are young and have thin cell walls with the lowest rhizodermic pH, which enhances Pb solubility in soil solution.

Table 2. Different indices used to quantify Lead toxicity at trophic levels in the food chain [18].

SN	Factors	Equations	References
1	Trophic transfer factor (TTF)	TTF = Pb conc. in organism tissue/Pb conc. in food	[75]
2	Transfer factor (TF)	TF = Pb conc. in plant tissue/Pb conc. in soil	[76]
3	Metal transfer factor (MTF)	MTF = Pb conc. in plant/Pb conc. in soil	[77]
4	Accumulation factor (AF)	AF = Pb conc. in plant edible part/Pb conc. in soil	[78]
5	Bioaccumulation factor (BAF)	BAF = Pb conc. in organism tissue/Pb conc. in abiotic medium	[79]
6	Bio-concentration factor (BCF)	BCF = (Pb conc. in experimental organism tissues − Pb conc. in the control organism tissues)/Pb conc. in water	[80]
7	Biota-sediments AF (BSAF)	BSAF = Pb conc. in the organism/Pb conc. in sediments	[81]
8	Biomagnification factor (BMF)	BMF = Pb conc. in the organism/Pb conc. in the organism's diet	[82]
9	Trophic magnification factor (TMF)	TMF is calculated from the slope of logarithmically transformed Pb conc. in organisms plotted against the trophic levels of the organisms in the food web	[83]

After entering into the roots, Pb moves by apoplast through water stream until it reaches the endodermis region. The endoderm functions as a physical barrier to Pb translocation as water stream is blocked by casparian strip and, thus, Pb enters into the symplastic movement. The low Pb transportation from root to APP has been reported due to immobilization by negatively charged pectins within the root cell wall [2,84]. Insoluble Pb salts precipitate in intercellular spaces of root cells [70,84]. Similarly, Pb accumulation in plasma membranes of root cells [61,84] or sequestration in the vacuoles of rhizodermal and cortical cells of roots is reported [68,84]. The major portion of the absorbed lead is sequestered/excreted from endodermis cells during the plant detoxification process. However, the above reasons are not sufficient to explain the low Pb translocation from root to APP as plant species such as *Brassica pekinensis* and *Pelargonium* potentially translocate Pb to APP, without affecting metabolic functions [85,86]. The lead hyper accumulator plant species can accumulate >1000 ppm [87]. The roots of hyperaccumulator species dissolve metals in soil [86], increase metal uptake and translocation, and make hyperaccumulator species to tolerate higher Pb ions concentrations. Apart from this, various detoxification mechanisms include selective metal uptake, excretion, complexation by specific ligands, and compartmentalization, which are also support for Pb tolerance.

In addition, Pb translocation to APP increases by organic chelators like ethylene diamine tetra acetate (EDTA) and micro-organisms [2,25]. Liu et al. [88] observed higher translocation to APP with increased soil Pb level in *B. Pekinensis* cultivars. This may be due to the potential of high Pb concentrations to destroy the casparian strip based physical barrier.

Xylem helps in the transportation of metals from plant roots to shoots [89], which is probably supported by transpiration [90]. Arias et al. [2] demonstrated X-ray mapping and found high Pb deposition in xylem and phloem cells on mesquite plants. After penetrating into the central cylinder of the stem, Pb can again be transported via the apoplastic pathway and further translocated to leaf areas through vascular flow [73]. In xylem, Pb can form complexes with amino/organic acids [87]. However, inorganic Pb can also be transferred. Translocation factor (i.e., lead in aerial parts/leading roots) can be implemented to know the degree of Pb translocation [86,88]. After implementing this factor, low numeric values will indicate that lead has been sequestered in the roots system [88].

The molecular mechanism of Pb entrance in roots is not clear yet. It is believed that several pathways can be used by Pb for the same purpose, especially ionic channels. However, Pb uptake is a non-selective phenomenon and is independent of the H^+/ATPase pump [91]. Lead absorption is inhibited by calcium [92] as Pb competes with Ca for calcium channels. Ca^{2+}-permeable channels are important gateways for Pb to penetrate into the root system [91,93]. The transgenic plant studies reveal that Pb can also penetrate into roots through other alternative non-selective pathways, e.g., cyclic nucleotide-gated ion channels and low-affinity cation transporters [94]. Comprehensive details for the average lead content in different food crop plants are summarized in Table 3. It is noted that higher concentrations of Pb are associated with fruit crops (Table 3).

Table 3. Details for the average lead contents in different crop plants.

Plant Species	Scientific Name	Concentration (mg/kg)	References
	Vegetable crops		
Coriander	*Coriandrum sativum*	4.5	[95]
Spinach	*Spinacia oleracea*	0.98–9.2	[96–99]
Coriander	*Coriandrum sativum*	0.4–75.5	[98,100–105]
Cabbage	*Brassica oleracea*	0.07–12	[97,104,106–108]
Radish leaf	*Raphanus sativus*	0.4	[100]
Amaranthus	*Amaranthus blitum*	23.26	[109]
Parsley	*Petroselimum crispum*	2.31	[97]
Slender amaranth	*Amaranthus viridis*	2.56	[101]
Sugar beet	*Beta vulgaris L*	149.5	[102]
Slender amaranth	*Amaranthus viridis*	5.44	[110]
Tomato	*Solanum lycopersicum*	5.5	[99]
Brinjal	*Solanum melongena*	2.1	[95]
Cucumber	*Cucumis sativus*	1.5	[95]
Brinjal	*Solanum lycopersicum*	2.2	[98]
Raddish	*Raphanus sativus*	0.75	[111]
Eggplant	*Solanum melongena*	4.93	[112]
Brinjal	*Solanum tuberosum*	6.19	[112]
Pumpkin	*Cucurbita maxima*	0.25	[113]
Chilli	*Capsicum annuum*	0.17	[113]
Carrot	*Daucus carota*	0.72–7.8	[95–97]
Sugar beet	*Beta vulgaris* L.	26.35	[109]
Potato	*Solanum tuberosum*	0.012–2.58	[106,107]
Cauliflower	*Brassica oleracea*	0.36–6.1	[95,97,104]
	Spices Crops		
Aniseed	*Pimpinella anisum*	0.26–5.68	[114,115]
Bay leaf	*Cinnamomum tamala*	0.98–3.58	[116–118]
Cardamom	*Elettaria cardamomum*	0.583	[115]
Cassia	*Cinnamonum cassia*	4.159	[115]
Curry	*Murraya koenigii*	3.617	[117]
Dill	*Anethum graveolens* L.	0.81	[119]
Fennel	*Foeniculum vulgare*	0.316	[115]
Fenugreek	*Trigonella foenum-graecum* L.	9.38	[114]
Rosemary	*Rosmarinus officinalis*	10.8	[120]
Tulsi	*Ocimum sanctum*	4.59	[116]
	Fruit Crops		
Mango	*Magnifera indica*	0.642–1.620	[121,122]
Orange	*Citrus sinensis*	26	[123]
Pomegranate	*Punica granatum*	28	
Grapes	*Vitis vinifera*	24	
Lemon	*Citrus limon*	29	
Strawberry	*Fragaria ananassa*	10	
Buckthorn	*Hippophae rhamnoides*	20	
Peaches	*Prunus persica*	11	

Table 3. *Cont.*

Plant Species	Scientific Name	Concentration (mg/kg)	References
Banana	*Musa* sp.	0.003–0.05	[122,124]
Jackfruit	*Artocarpus heterophyllus*	0.017	
Orange	*Citrus sinensis*	0.106	[125]
Trengerine	*Citrus tangernia*	0.097	
Banana	*Musa*	0.118	
Papaw	*Carica papaya*	0.072	
Cereals and Legumes Crops			
Pearl millet	*Pennisetum glaucum*	0.12	[126]
Sorghum	*Sorghum bicolor*	0.18	[126]
Wheat	*Triticum aestivum*	0.40	[127]
		0.47	[128]
Barley	*Hordeum vulgare*	0.22	[129]
Quinoa	*Chenopodium quinoa*	0.37	[130]
Maize	*Zea mays*	0.50	[131]
		0.34	[132]
		0.31	[133]
Rice	*Oryza sativa*	0.52	[134]
		0.89	[135]
Black gram	*Vigna mungo*	0.60	[133]
Lentil	*Lens culinaris*	0.55	[133]
Common bean	*Phaseolus vulgaris*	0.12	[136]
Soybean	*Glycine max*	0.08	[137]
Safflower	*Carthamus Tinctorius*	0.80	[138]
Rapeseed	*Brassica napus*	0.51	[138]
Sunflower	*Helianthus annus*	0.57	[131]

Accidental soil ingestion is a major Pb exposure pathway for humans inhabited in a Pb polluted area [9,139]. However, the intake of Pb contaminated plants has been an important exposure to humans and animals [9,139,140]. Edible/wild plants cultivated/grown in the vicinity of phosphate industries can be Pb bio-indicators of toxic metals [9]. Inhabitants and workers of these industries/provinces may be exposed to Pb contamination. The Pb exposures and blood concentration to these closely inhabited/living populations is subject to the season as well as industrial activity. The children's blood lead levels (BLLs) were observed to be higher during the summer and early fall [141]. The BLLs are highly significant, are evident in multiple locations, periods, and ages, and are population-specific [142,143]. Higher levels were observed (10–60%) in warm-weather and levels increased in 2-year-old children, more so than 1 or over 4-year-olds [142,143]. Zahran et al. [143] emphasized that lead seasonality must be considered for Pb risk analysis. One health concept was proposed to take care of animal, human, and environmental health all together [144,145].

7. Mechanistic Understanding of Pb Toxicity and Tolerance in Plants and Humans

Lead causes a broad range (physiological, morphological, and biochemical) of toxic effects on living organism. In plants, Pb toxicity is characterized with impaired chlorophyll (Chl a) production, cell division, elongation of root, lamellar organization in the chloroplast, plant growth, seed germination, seedling development, and transpiration [67,87]. However, the magnitude of the effects varies and/or depends on Pb levels, exposure time, plant stress intensity, and plant developmental stage. Plants have internal detoxification mechanisms to deal with Pb toxicity, i.e., complexation by specific ligands, selective metal uptake, excretion, and compartmentalization [18,21,61,87].

Lead induced oxidative stress is reported to produce reactive oxygen species (ROS) in plants [146,147]. These ROS synthesized as a result of oxidative stress in plants can cause deleterious effects such as lipid peroxidation, disrupted cell membrane, DNA and protein damage, inhibition of photosynthesis, and inhibition of ATP production [148]. To overcome the adverse effects of ROS, plants produce a variety of antioxidative enzymes. Lead imposed changes in antioxidative enzyme production of various food crops have been well established (Table 4). The activity of antioxidative enzymes, such as superoxide dismutase, peroxidase, and ascorbate peroxidase, were positively correlated with Pb content, while Catalase, Glutathione reductase, and Glutathione peroxidise were decreased in both leaf and root tissues (Table 4).

Lead poisoning cases in humans are mostly the result of oral ingestion and absorption via the gut [149]. Pb absorption from the gastrointestinal tract is subject to physical characteristics (such as age, pregnancy, fasting, and Fe and Ca status) and the physico-chemical nature of the material ingested (e.g., size of particles, solubility, mineralogy, and Pb species) [150]. The Pb absorbed in the intestine is further carried to soft tissue, e.g., in the liver, kidneys, and bone tissue, where it accumulates over time [149]. The main transport processfor Pb to different body tissues from the intestine is via red blood cells, where binding takes place between Pb and haemoglobin (HB). Nearly 99% of the Pb in blood is observed in erythrocytes, with approximately 1% in both serum and plasma. Distribution of Pb in the organs (the lungs, spleen, brain, aorta, renal cortex, bones, and teeth) relies greatly on Pb concentration in plasma rather than on the whole blood. The half-life of Pb in blood is estimated to be 35 days, whereas the half-life of Pb in soft tissue is estimated to be 40 days. Pb can be resident in bone for up to 30 years and concentrations of Pb in teeth and bone grow in proportion to age [149]. The Pb biological half-time is believed to be significantly greater in children than in adults. Lead creates chemical bonds with thiol groups of proteins and Pb toxicity is believed to inhibit enzymes and subsequently interfere with homeostasis of Mg, Ca, and Zn. Lead-induced oxidative stress is caused due to Pb poisoning as it disrupts the pro-oxidant/antioxidant cell defence system. Antioxidant nutrients, such as vitamins E, C, B_6, and B-carotene, and also Zn and Se, are believed to combat Pb-induced oxidative stress [151].

High levels of Pb absorption are found in children rather than in adults. It is approximated that adults may absorb 3–10% of an oral dose of water-soluble Pb, whereas for children, it may be as high as 40–50%. Higher Pb concentrations are found in the blood of children who are Fe- or Ca-deficient than those with replete Fe or Ca. Pb absorption may raise during the pregnancy period and over 95% of Pb deposits in skeletal bones as insoluble phosphate [149]. According to autopsy studies, cortical bone and teeth together account for 90–95% of the body's Pb burden. The total Pb body burden in the skeleton is 80–95% in adults and about 73% in children [149]. Mothers may transfer Pb to the foetus and also to infants during the period of breastfeeding [152]. Pb toxicity principally targets the human central nervous system and children's ingestion of large amounts of Pb from the environment, particularly when anaemic, is linked to lower intelligence and impaired motor function [149].

The Joint FAO/WHO Expert Committee on Food Additives (JECFA) made an estimation of tolerable weekly intake based on dose-response analyses and concluded that the provisional tolerable weekly intake (PTWI) is linked to a reduction in children's IQ of at least 3 points and systolic blood pressure of approximately 3 mmHg (0.4 kPA) higher in adults [149]. When observed in terms of a shift in IQ distribution or blood pressure in a population, these changes assume greater importance. The JECFA's conclusion, therefore, was that the PTWI is no longer adequately protective of health and they withdrew it. The lack of an indication of a threshold level for key effects of Pb based on the dose-response analysis led the JECFA to conclude that a new PTWI considered as health-protective could not be established. The JECFA reiterated that foetuses, infants, and children are the subgroups that have the highest sensitivity to Pb [150,153] due to the neuro-developmental effects. The European Commission [154] has set guidelines for maximum permissible levels of Pb in some foodstuffs (Table 5). Interventions such as eliminating leaded petrol, banning the use of Pb in wine bottles, and the discontinuation of soldered cans are seen as an important factor in successful reduction of Pb in food. In children, Pb toxicity symptoms are loss of appetite, anemia, behavioral changes, delayed mental growth and learning, fatigue, headaches, hyperactivity, insomnia, metallic taste, reduced nerve conduction, weight loss, and possibly neuron disorders [155]. The behavior changes are irreversible and untreatable as the cerebrum of *Homo sapiens* has little capability for reparation. A daily Pb intake of up to 7 µg/kg body weight or 490 µg of Pb for an adult was accepted by WHO, FAO. However, no such guideline is given for infants and children, who are relatively more sensitive to low Pb levels [156].

In broilers that have high Pb acetate (200 mg/kg) exposure in their diet, these show anorexia, greenish diarrhea, leg paresis, weight loss, wing droop, and lethargy symptoms including gross change in kidney, spleen, and liver function, gizzard lining, hemorrhages on muscles [157], etc. Gao et al. [157] concluded that Pb could alter the expression of selenoprotein related genes in the cartilage tissue of broilers. Rahman and Joshi [158] revealed that Pb acetate (i.e., 250–400) in drinking water could lead to reduced feed intake and growth indices in broilers due to higher oxidative stress. Pb-induced oxidative stress can also reduce antioxidant activities such as catalase, glutathione superoxide dismutase [159], etc. and erythrocytes burst due to lipid peroxidation in erythrocytes membranes and may cause hemolytic anemia [160]. Pb could also respond to change in the activities and expression of antioxidant enzyme–related genes [161,162]. Most animal experiments confirm that Pb transportation in the body occurs through blood circulation and accumulates in soft tissues, bones, and other pivotal organs [163]. Bones are a major sink of Pb (~90%) and mostly replace calcium, thus decreasing in bone mineral density (BMD) due to Pb exposure [164].

Table 4. Effects of Pb toxicity on activities of different antioxidant enzymes in different plants [16].

	Enzymes		**Pb Exposure Level**	**Duration**	**References**
	Enhanced	**Reduced**			
Sedum alfredii	SOD	APX	0–200 µM	14	[63]
Triticum aestivum	SOD, POX, APX	CAT	0, 0.15, 0.3, 1.5, 3.0 mM	6	[165]
	SOD, POX, CAT, APX	-	0, 1, 2, 4 mM	3	[166]
	SOD, CAT	APX, GPX, GR	0, 8, 40 mg L^{-1}	5	[167]
	SOD	GPX	0, 500, 1000, 2500 µM	7	[168]
Oryza sativa	SOD	CAT, POD	0, 50, 100, 200 M	16	[169]
Triticum aestivum	SOD, CAT	APX, GPX, GR	0, 50, 100, 250, 500 µM	4	[170]
Zea mays	SOD, APX, GPX, GR	CAT	0, 16, 40, 80 mg L^{-1} Pb^{2+}	8	[146]
	APX, DHAR, MDHAR	-	0, 16, 40, 80 mg L^{-1} Pb^{2+}	1	[171]
Oryza sativa	SOD, APX, GR	CAT	0, 10, 50 µM	4	[172]

SOD: Superoxide dismutase; POX: Peroxidase; APX: Ascorbate peroxidase; CAT: Catalase; GPX: Glutathione peroxidise; GR: Glutathione reductase; MDHAR: monodehydroascorbate reductase; DHAR: dehydroascorbate reductase.

Table 5. Maximum permissible level of Pb in foodstuffs (mg/kg Fresh Weight).

Lead in Food Stuffs (mg/kg Fresh Weight)	**Maximum Permissible Level**
Food of Plant Origin	
Rye, grain	0.20
Wheat, grain	0.20
Bread	-
Miscellaneous cereals	-
Cabbage	0.30
Carrot and potatoes	0.10
Apple	0.10
Milk chocolate	-
Food of animal origin	
Carcass meat	0.10
Offal	-
Fish	0.30
Fresh water fish,	0.30
Eggs	-
Milk	0.02
Dairy products	-

8. Human Health Effects Due to the Consumption of Pb Contaminated Foodstuffs

Lead enters into the body through pathways like inhalation of wind-blown Pb-laden dust, ingestion of Pb contaminated soils, oral intake of Pb contaminated water, and food grown in Pb-contaminated areas. Pb accumulation in livestock tissues may also pose a major risk to human health through livestock meat consumption [173,174]. After absorption, Pb is distributed in the body through red blood cells (RBC). Pb is mostly bound to hemoglobin rather than RBC membrane after entering the cell [175]. The hematopoietic is a sensitive system for critical Pb toxicity and may lead to anemia [160]. Histopathological observations confirmed that Pb ions are transported to the liver, where they can induce chronic damage to the liver. Pb toxicity also increases blood enzyme levels and reduces protein synthesis [176–178]. Pb imposes toxic effects on kidneys through structural damage and changes in the excretory function [176,177,179]. The other organ and tissue systems affected due to lead toxicity are the nervous, cardiovascular, and reproductive systems [160,175,180]. Pb toxicity imposes mineralizing of bones and teeth, which is a major body burden [3]. The International Agency for Research on Cancer (IARC) stated that inorganic Pb is probably carcinogenic to humans (Group 2A) based on limited evidence in humans and sufficient evidence in animals [181]. Generalized clinical symptoms of Pb poisoning in humans are comprehensively summarized in Table 6.

Table 6. Generalized clinical symptoms of Pb poisoning in humans.

SL No.	Body Organ/System	Clinical Symptoms of Pb Poisoning
1	Eyes	Blindness of parts of visual field Hallucinations
2	Ears	Hearing loss
3	Mouth	Unusual taste Slurred speech Blue line along the gum
4	Kidney	Structural damage and failure Changes in the excretory function
5	Liver	Jaundice Lead-induced oxidative stress Decreased liver function Microvesicular and macrovesicular steatosis Hemosiderosis and cholestasis
6	Skin	Pallor and/or lividity
7	Central nervous system (CNS)	Insomnia Loss of appetite Decreased libido Depression Irritability Cognitive deficits Memory loss Headache Personality changes Delirium Coma Encephalopathy
8	Reproductive organs	Sperm dysfunctions Pregnancy complications Preterm birth
9	Abdomen/Stomach	Pain Nausea Diarrhoea Constipation

Table 6. *Cont.*

SL No.	Body Organ/System	Clinical Symptoms of Pb Poisoning
10	Blood	Anaemia
11	General	Malaise Fatigue Weight loss
12	Neuro- muscular	Tremor Pain Delayed reaction times Loss of coordination Convulsions Foot or ankle drop Seizers Weakness
13	Bones	Mineralizing bones and teeth Decreased bone density

9. Pb Remediation approaches

Innovative and site-specific Pb remediation technologies for efficient clean-up of contaminated sites are prerequisites for a healthy life and safe food production. There are different (physical, chemical, and biological) processes developed to reduce total Pb concentration and Pb bioavailability to mitigate Pb accumulation in the food chain [182,183].

9.1. Physical Approaches

9.1.1. Replacement of the Medium (Soil/Water)

In this method, the complete or partial replacement of the contaminated resources (soil/water) is done based on the magnitude of the contamination [183]. This method of remediation is very useful at a small scale at the local level. The biggest challenge for this method is the safe disposal of the contaminated soil/water in a cost-effective manner.

9.1.2. Vitrification

This method can be applied through both in-situ and ex-situ remediation mechanisms. In vitrification methods, soil is melted with the help of a high-temperature process and Pb sequestration achieved in solidified vitreous mass [183,184]. Vitrification can be used long-term and effective low volume can be obtained for reuse [183]. This is a costly method and may not be suitable for applications in large areas. Dellisanti et al. [185] carried out the vitrification of Pb-rich ceramic waste. Wang et al. [186] treated fly ash from a municipal solid waste incinerator to radiated heavy metals including Pb. Navarro et al. [187] applied vitrification for remediating the hazardous mine wastes from old mercury and Ag-Pb mines in Spain.

9.1.3. Electrokinetic Remediation

Electrokinetic remediation is achieved by applying current in the field. This process involves techniques such as electrophoresis, electric seepage/electro-migration, electro-osmosis, and electrolysis [188]. Kim et al. [189] has shown that contaminated rice soil could be cleaned using an electrokinetic technique, which reduces Pb contamination by 19.4% in 4 weeks. Jeon et al. [190] remediated a soil contaminated with Pb in a paddy rice crop using EDTA as an electrolyte. The electrokinetic remediation technique generates almost nil waste. Electrokinetic remediation is applicable for saturated soils with low groundwater flow, requires short repair time and low energy, and provides a complete repair [183]. The heterogeneity of soil and treatment depths are the two important limitations of this method.

9.2. Chemical Approaches

Various chemical amendments are widely used for immobilization of lead in soil and ground water at the field scale (Table 7).

9.2.1. Chemical stabilization

This method is used to decrease the mobility, bioavailability, and bio-accessibility of heavy metals in soil. The immobilizing agents, i.e., biochar (Wheat, Rice, Miscanthus straw biochar, Sugarcane bagasse biochar, Holm oak chips biochar), clay minerals (Sepiolite with limestone, Palygorskite, and Bentonite), liming materials (Oyster shells and eggshells), metal oxides (Mn oxides and Ferric oxyhydroxide powder with limestone), organic composts (Biosolid), and phosphate compounds (Phosphate rock, Calcium magnesium Phosphate, and Single superphosphate) were previously used in the chemical stabilization process [183], details of which are given in Table 7. Chemical stabilization is a simple, quick, relatively cost-effective chemical approach by which Pb can be immobilized by adsorption, chemical precipitation, ion exchange, and surface complexation mechanisms to limit Pb transport and bioavailability. However, in this process, Pb remains in the soil and hence, long-term immobility is recommended.

9.2.2. Solidification/Stabilization

Solidification/stabilization (waste fixation) is relatively low cost, low risk, easily implemented, and highly resistant to biodegradation with abroad engineering applicability [183]. Soil solidification refers to the encapsulation of waste materials in a monolithic solid with high structural integrity [183,191]. Soil stabilization is achieved by stabilization of soil contaminants through chemical interaction between Pb and binding reagents [192]. Wang et al. [193] and Antemir et al. [194] demonstrated the potential cement-based binders in remediating heavy metals including Pb in England. Navarro-Blasco et al. [195] assessed the Pb adsorption capacities of calcium aluminate cement. Voglar and Lestan [196] used calcium aluminate cement and sulfate resistant Portland cement as binders for Pb immobilization in Slovenian soil. Wang et al. [197] assessed Portland cement, ground granulated blast furnace slag, pulverized fuel ash, MgO, and zeolite for on-site soil solidification/stabilization of Pb in UK soil.

9.2.3. Soil Washing

The soil washing process is achieved by Pb leaching from soil matrix using reagents/extractants such as chelating agents, inorganic acids, organic acids, surfactants, and water. The soil mixing with respective reagents/extractants is done where extractants transfer Pb from soil to the liquid phase through chelation or desorption, chemical dissolution, and ion exchange mechanisms [198]. Soil washing is a rapid, permanent, effective chemical method for Pb remediation with long term liability [199]. Hu et al. [200] achieved removal of 73% Pb using EDTA as a chelating agent. Wang et al. [201] used iminodisuccinic acid, glutamate-N, N-diacetic acid, glucomonocarbonic acid, and polyaspartic acid to extract 53% and 55% Pb from Pb-Zn contaminated soil. However, these technologies have certain hurdles for their practical utility due to change in soil properties, loss of nutrients, adverse effect of washing chemicals, generation of wastewater, and cost of chemicals and their negative impact on the environment.

9.3. Biological Approaches

Biological methods for Pb remediation are the most eco-friendly alternatives to remediate Pb from the contaminated resources. Biological remediation can be referred as direct utilization of any natural/genetically engineered living organism and their product for Pb detoxification to restore soil function and quality.

Table 7. Chemical amendments for immobilization of lead in soil and groundwater at the field scale [183].

SN	Amendments	Immobilization Mechanisms	Observations	Reference
1.	Clay minerals			
	Sepiolite + limestone	Chemical precipitation and surface complexation	The treatment decreased exchangeable Pb (99.8%) and reduced Pb in brown rice (81.2%).	[202]
			The treatment significantly increased soil pH and CEC, decreased Pb exchangeable fractions, and inhibited Pb accumulation in rice.	[203]
	Palygorskite		Significantly reduced water leachable Pb fractions (50%).	[204]
	Bentonite		Reduced Pb exchangeable fractions (20.3–49.3%). Increased residual portions (6.73–10.0%). Pb concentrations in the rice roots (5.13–26.7%) and shoot (3.73–7.8%) were reduced.	[205]
2.	Phosphate compounds			
	Phosphate rock (Ca$_{10}$(PO$_4$)6Cl$_2$ Calcium magnesium phosphate (Ca$_3$(PO$_4$)$_2$) Single superphosphate (Ca(H$_2$PO$_4$)$_2$)	Pb: Pb phosphate precipitation, especially pyromorphite-like mineral;	P fertilizers decreased water soluble and exchangeable Pb fractions (22.03–81.4%) and reduced Pb uptakes (16.03–58.0%) by a Chinese green vegetable.	[206]
3.	Liming materials			
	Oyster shells and egg shells	Chemical precipitation	TCLP-leachable Pb was effectively reduced.	[207]
4.	Organic composts			
	Biosolid	Surface complexation and chemical precipitation	The treatment enhanced soil pH, cation exchange capacity, and humic acids, with improved soil sorption capacity. The readily soluble Pb forms were reduced.	[208]
5.	Metal oxides			
	Ferric oxyhydroxide powder + limestone	Specific sorption, co-precipitation, and inner-sphere complex	Pb decreased by 97% in pore water. Pb was transformed into residual mineral.	[209]
	Mn oxides		Pb immobilization.	[210]
6.	Biochar			
	Wheat Straw Biochar	Increase in soil pH, total organic carbon, abundant functional groups, and complex structures of biochar leads to reduction in heavy metals extractable fractions	The soil extractable Pb was decreased. As a result, Pb in root tissues was significantly reduced.	[211]
			Biochar significantly transformed the exchangeable Pb fractions into relatively stable fractions.	[212]
	Sugarcane bagasse biochar		The exchangeable Pb was reduced and the organically-bound fraction increased with increased biochar input. Pb bioavailability to plant shoots and roots decreased with increasing biochar input.	[213]

Table 7. *Cont.*

SN	Amendments	Immobilization Mechanisms	Observations	Reference
	Holm oak chips biochar		Biochar stabilized Pb and reduced its accumulation in barley grain.	[214]
	Rice straw biochar		Rice straw biochar decreased. Pb bioavailability and reduced Pb contents in vegetables.	[215]
	Miscanthus (Miscanthus giganteus) straw biochar		$CaCl_2$-extractability of Pb significantly decreased with increased biochar input.	[216]

9.3.1. Phytoremediation

Phytoremediation is an environmentally-friendly, attractive, aesthetically pleasing, noninvasive, energy-efficient, and cost-effective technology that can remediate Pb in low to moderate contaminated soil. It includes phytostabilization and phytoextraction. Phytostabilization decreases the mobility/ bioavailability of Pb through adsorption by roots, chemical precipitation, and complexation in the root zone. Phytostabilization is only effective up to the root depth of plants. Cheng et al. [217] observed the Pb phytoremediation potential of *Miscanthus floridulus.* Yang et al. [218] ascertained the phyto-extraction potential of a co-planting system of *Pteris vittata* L. and the *Ricinus communis* L. in Pb contaminated soil and observed an increased yield of *P. vittata* after Pb uptake. Metal hyper accumulater plant species such as *Eichhornia crassipes*, *Lemna* sp., *and Pistia stratiotes* have been widely used to remediate Pb from diversified environments (Table 8).

9.3.2. Microbial Remediation

Microbial remediation refers to decreasing the availability of Pb in the environment using indigenous/exotic microbes. Bacterial species such as *Alcaligenes* sp., *Bacillus firmus*, *Bacillus licheniformis*, *Enterobacter cloacae*, *Escherichia coli*, *Micrococcus luteus*, *Pseudomonas fluorescens*, and *Salmonella typhi* show adsorption potential of Pb from the contaminated resources [219–223]. Wang et al. [224] concluded that bacterial strain B38 (mutant of *Bacillus subtilis*) has immense potential to remediate heavy metals including Pb in China. Zeng et al. [225] observed that *Aspergillus niger* strain SY1 effectively removed Pb (99.5%) from contaminated sediment through bioleaching. The fungal biomass of *Lepiotahystrix*, *Aspergillus niger*, *Aspergillus terreus*, and *Trichoderma longibrachiatum* are reported as potential bio-sorbents [223,226,227]. The algal species i.e., *Palmaria palmate*, *Spirulina maxima*, *Spirogyra hyaline*, *Cystoseira barbata*, *Cladophora* sp., *Chara aculeolata*, *Nitella opaca*, and *Ulva lactuca* are were identified to be efficient bio-sorbents [223,228,229]. Microbial remediation is considered to be a natural, safe, and effective eco-friendly technology with low energy and low operation cost inputs [183]. Most importantly, microbial remediation does not impose any environmental and health hazards. The process depends on the environmental condition and inputs such as nutrients, oxygen, and other amendments to stimulate microbial activity for Pb remediation [183].

9.3.3. Microbial Assisted Phytoremediation

Many approaches including molecular fingerprinting techniques *viz.* length heterogeneity analysis by PCR (LH-PCR), terminal restriction fragment length polymorphism (T-RFLP), denaturing gradient gel electrophoresis (DGGE), single strand conformation polymorphism (SSCP), ribosomal intergenic spacer analysis (RISA), cloning, and In Situ Hybridization (ISH/FISH) were used to identify the potent microbial community involved in phytoremediation [230–234]. This approach is based on the rhizosphere associated microbes such as *Bacillus*, *Beijerinckia*, *Burkholderia*, *Enterobacter*, *Erwinia*, *Flavobacterium*, *Gluconacetobacter*, *Klebsiella*, *Pseudomonas*, *and Serratia* [235–237]. Babu et al. [235] inoculated soil with rhizospheric bacteria *Pinus sylvestris* and found significant increases in biomass, chlorophyll content, nodule number, and Pb accumulation in *Alnus firma* seedlings.

Table 8. Phytoremediation potential of different plant species for Pb contaminated water and soil [21].

Species	Treatments	Observation	Findings	References
Ceratophyllum demersum	Artificial wastewater	Removal rate 92.0–95.0%	Maximum BCF of 1284.35 in 4 mg/L of Pb 12th Day.	[238]
Leptodictyum riparium	Artificial wastewater	Removal rate 96.7%	Having high resistance and effectiveness for Pb accumulation.	[239]
Scirpus grossus	600 L spiked water in Pb (10, 30, and 50 mg/L), duration 98 days	Pb concentration in water decreased up to 99% after 28 days and highest Pb uptake: 1343, 4909, 3236 mg/kg for the treatment of 10, 30, and 50 mg/L Pb, respectively	Highest BCF and TF were 485, 261, and 2.52 on day 42 of Pb treatment at 30 mg/L concentration in 70 days retention time.	[240]
Pistia stratiotes	Greenhouse condition using glass pots with a defined amount of added HMs	Pb removal was >90% in the first week	No enhancement of Pb removal efficiency with increased Pb concentrations.	[241]
Eichhornia crassipes	Operation in up-flow anaerobic packed bed reactors system	Pb Removal rate: 98%	In the coupled pond system, water hyacinth was observed to have enhanced Pb removal efficiency by accumulating Pb into root	[242,243]
Eichhornia crassipes	Stock solutions with initial concentration of 20 g/L	Pb Removal rate: 98.33%	Powdered root of water hyacinth absorbed higher Pb.	[244,245]
Brassica oleracea var. Acephala	Treatments of different Concentration Pb = 0, 1, 5, and 10 mg/kg	Phytoremediation of saline soils with 10 and 16 mg/kg Pb	Negatively correlated with plant fresh and dry weights.	[246]
Posidonia oceanica	Sediments	Pb Levels (mg/kg) in root: 4.52 ± 0.55,	Ability of *Posidonia oceanic* to accumulate and detoxify Pb rather than being attributed to differences in ecological and morpho-anatomical characteristics.	[247]
Datura inoxia	Concentrations of 0.5, 1.0, 3.0, 5.0, 10, 15, 20, 25, 30, 35, 40, 45, 50 mg/L metal	Survival rate = 50%	*Datura* exhibits phytoremediation potential.	[248]
Magnolia grandiflora	Soil	Pb Accumulation rate: 63.4%,	Relationship between heavy metal concentrations in soils and washed new and old leaves.	[249]
Pistia stratiotes	HMs from steel effluents: 120 g of plant in 10 L effluent	Removal rates: Pb = 70.7%,	*E. crassipes* more efficient than *P. stratiotes.*	[250]
Lemna sp.	Artificial by concentration of 2, 5, and 10 mg/L	Pb removal rates by *Lemna gibba*: 60.1% at 2 mg/L at pH 9, 98.1% at 10 mg/L at pH 7,	BCF and metal uptake yield per unit of dry biomass for Pb is 403–738.	[251]

Table 8. *Cont.*

Species	Treatments	Observation	Findings	References
Pistia stratiotes	Stock solution (2000 mg/L)	96% removal of Pb(II) from 25 mL of solution in 60 min by only 0.125 g of biomass	Results consistent with the Langmuir model by maximum biosorption capacity of 122.70 mg Pb (II)/g of biomass.	[252]
Mixture of Typha angustifolia and Limnocharis flava	Wastewater oxidation pond	Removal rate: Pb = 62.07%	Positive relation between retention time and heavy metal removal.	[253]
Lemna sp.	200 g fresh plant in mixed sewage of industrial and municipal effluents	Pb Removal efficiency >80%	BCFs for Pb = 523, indicating that this plant is a moderate accumulator of Pb.	[254]
Lemna sp.	Artificial: Pb = 0.25 mg/L	Removal rates: Pb = 36%	Removal efficiency up to 80% at higher metal loading rate where 24 h light and pre-treatment steps required.	[242,243]
Eichhornia crassipes	Mining wastewater	Accumulation in leaves (mg/kg): Pb = 3.40–5.06	BCF: Pb = 242–506	[255]
Mixture of P. australis and T. latifolia	Urban sewage mixed with industrial effluents	Removal rate: Pb = 61.0 ± 1.2%	-	[256]

9.4. Biotechnological and Genetic Approaches

Genomics, metagenomics, metabolomics, proteomics, transcriptomics, nanoparticles, and isotope probing are modern technologies to understand Pb phytoremediation [234,235,257]. The biotechnology and genetic approaches to remediate Pb from the contaminated resources have great potential and have been proved in some plants [19]. Hattab et al. [258] observed a significant increase in ROS and cellular oxidative stress in *Medicago sativa* through influencing the expression of CuZn-SOD, GSH synthase (GS), and GPX against Pb stress. Fan et al. [259] observed an unknown protein, product of PSE1 (Pb-sensitive1) gene with NC domain, which is localized in cytoplasm and has potential for Pb tolerance in *A. thaliana*. Jiang et al. [260] studied the role of PDR12 knockout *Arabidopsis* and under Pb stress conditions and concluded that PDR12 is responsible for the activation of a Pb exclusion mechanism. ABC transporter of the mitochondria 3 (ATM3) [260–262], acyl-CoA-binding protein [263], and leucine-rich repeat2 (LRR2) and ethylene-insensitive 2 (EIN2) [264] are also important to regulate Pb transportation to the exterior of the cell [19,265]. A cytosol-localized malate dehydrogenase (CMDH4) protein functions as regulation of Pb tolerance mechanisms [19,266]. Pb is easily affected by GSH reductase in the plant cell [267]. Pb-mediated increased expression phytochelatins were also observed in *Salvinia minima* [268]. *M. sativa* plants showed 23-fold increased expression of PCS gene in the presence of Pb [258]. Furthermore, GMO plants develop efficient metabolic processes and over express genes/enzymes that are capable of bioremediation specific pollutant. Different omic-approaches help to explore different potential solutions targeting precise pollutants. For utilizing the omic-approaches below, certain research should be covered:

(a) Identification of candidate genes for effective and efficient removal of Pb contaminants.
(b) Diversity and phylogenetic studies of gene and protein sequences which control Pb bioremediation.
(c) Development of Genetically modified organism (GMO) plants through transgenesis.

GMO plants are capable of remediating various waste effluents and polluted lands and could be advantageous for bioremediation practical applications. Moreover, information on the fundamental omic-approaches concerned in bioremediation can also contribute towards the development of efficient bioremediation systems. Besides that, analysis of comparative genomic and proteomic study, their functional variations, as well as evolutionary relationships existing between them can contribute towards designing new efficient bioremediation systems. Systems biology information like molecular pathways, gene ontogeny analysis, co-expression, and protein-protein interactions can influence the Pb bioremediation processes. Therefore, with the help of bioinformatic analyses and modern biotechnological techniques, one can evaluate and justify the need for genetically modified organisms for the development of efficient remediation systems in the near future (Figure 1).

9.5. Nano-Technological Approaches

Recent scientific development in nanoscience research opens the way to cost-effective, eco-friendly, and sustainable remediation approaches. A nano technological approach has been successfully used in soil, sediments, solid waste, and a wastewater remediation [18,269] process. Nano-materials are dynamic, efficient, and broadly applicable with economic expediency [18,270]. The characteristic features of nano-materials such as Nanocatalysts, CNTs, graphenes, nano-scale metal oxides, nanomembranes, carbon nanotubes, nanobiological processes and zero-valent iron (FeO), Fe_2O_3, Fe_3O_4, TiO_2, SiO_2, and Al_2O_3 are summarized in Table 9. Nanoparticles (1–100 nm) provide very high adaptability for both in-situ and ex-situ remediation approaches [18]. Nanomaterials, nanoadsorbents, and nanosized compounds (quantum dots, nanofilms, nanoparticles, nanotubes, nanowires, and other various colloids) used for Pb remediation are listed in Table 9. Nanoparticles (less than 50 nm) have high potential as Pb adsorbents. Nano-adsorbents, i.e., activated carbon, alginate biopolymer, clay materials, silica, magnetic iron oxide nanoparticles (MNPs), metal oxides, nano-titanates, etc. have been utilized to remove Pb [18,271,272]. The researchers showed that nano-material can enhance the accumulation of metals by improving the cell wall permeability, co-transportation of nanomaterials with heavy metals, and transporter gene regulation [18,273].

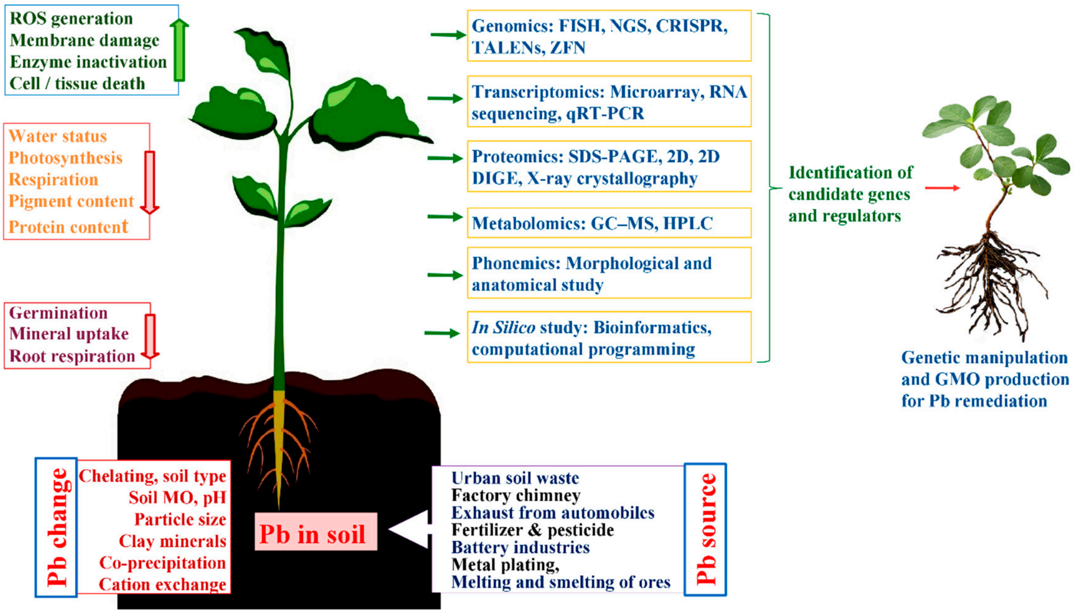

Figure 1. Biotechnological and Genetic Approaches for the development of efficient remediation systems.

Table 9. Characteristics of nano-particles in Pb removal [18].

SN	Nano-Particles	Characters	NP Synthesis	Absorbent Dose	Optimum pH	Removal Efficiency	References
1	Iron oxides NPs	Magnetite nanoparticles	Co-precipitation from a mixture of Fe(II) and (III) salts with aqueous NH_3 and KOH	50 mg/20cm^3	5.31–9.37	Pb(II)—76–92%	[274]
2	Ferrite nano particles	-	Modified co-precipitation synthesis	0.008	-	Pb(II) up to 38.1%	[275]
3	Activated carbon NPs	High surface area and greater adsorption capacity	-	0.02	2–10	Pb up to 87%	[276]
4	Nano scale zero valentiron (nZVI)	High surface area and cation exchange capacity	Reduction of Fe(II) using borohydride	-	-	-	[277]
5	Starch stabilized zero valent Iron nanoparticles(nZVI-Starch)	Larger surface area for sorption reactions	Chemical reduction method	1 g/kg soil	4.2	100%	[278]
6	Zeolite materials obtained from fly ash	Greater specific area	Hydrothermal process	6.0	5.6–6.6	>80%	[279]
7	Pyromellitic acid dianhydride/N-(3-(trimethoxysilyl) propylethylene diamine(PMDA/TMSPEDA)	Bound heavy metal ions via co-ordinate and electrostatic interactions	Ring opening polymerization and sol-gel reaction	0.01	7	Pd(II)—79.60%	[280]
8	Ag and Zn nanoparticles functionalized cellulose	High catalytic activity, great biocompatibility, high adsorption capacity, high surface-area, reusability, and greater dispersion degree	Co-precipitation method	0.5 and 1.0	5.5	-	[281]

Table 9. *Cont.*

SN	Nano-Particles	Characters	NP Synthesis	Absorbent Dose	Optimum pH	Removal Efficiency	References
9	ZnO@Chitosancoreshell Nanocomposite (ZOCS)	Hydrophilicity, biocompatibility, biodegradability, non-toxicity, and High adsorption capacity	Direct precipitation followed by thermal decarbonation	0.02	6	Pb(II) up to 99%	[282]
10	ZnO-Fe_3O_4 nanocomposites	High adsorption capacity and surface area	Chemical co-precipitation	0.50	5.5	Pb(II) up to 39.2%	[283]

10. Conclusion and Future Prospects

The source, bioaccumulation, and health hazards of Pb are due to industrial and agricultural activities. Translocation of Pb from soil to a crop system is a complex and species dependent phenomenon. The human consumptive plant species have shown different bioaccumulation, tolerance, and toxicity levels for lead. Based on the tolerance mechanism, different concentrations of Pb accumulate in the food chain and cause different magnitudes of human health hazards. To minimize these Pb based health risks, different remediation options are available for reducing the concentration of heavy metals in soil and the food chain. However, site and source-specific integrated approaches must be practiced to formulate suitable remediation strategies. Biological remediation, such as phytoremediation and PGPR, can be an environmentally friendly and cost-effective strategy for alleviating Pb toxicity in moderately contaminated soils. Eco-feasible technological innovations such as nano-tools and awareness among farmers' fraternity could possibly boost local economies and livelihoods with certain financial guarantees. Similarly, suggestive measures should be taken to ensure the sustained efficacy of Pb remediation such as the development of promising plants/mechanisms suitable for Pb phytoremediation. Exploitation of molecular approaches is required to manipulate Pb transporters and their cellular targeting to specific cell types. Development of transgenic plants with enhanced plant-microbe interaction is also a viable option to enhance phyto-remediation of Pb.

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