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Posted Date: 6 May 2023

doi: 10.20944/preprints202305.0398.v1

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Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 6 May 2023 doi:10.20944/preprints202305.0398.v1

Review

Heavy Metal Contamination in Agricultural Soil: Environmental Pollutants Affecting Crop Health

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Abstract: Heavy metals and metalloids (HMs) are environmental pollutants, most notably cadmium, lead, arsenic, mercury, and chromium. When HMs accumulate to toxic levels in agricultural soils, these non-biodegradable elements adversely affect crop health and productivity. The toxicity of HMs on crops depends upon factors including crop type, growth condition, and developmental stage; nature of toxicity of the specific elements involved; soil physical and chemical properties; occurrence and bioavailability of HM ions in the soil solution; and soil rhizosphere chemistry. HMs can disrupt normal structure and function of cellular components and impede various metabolic and developmental processes. This review evaluates: (1) HM contamination in arable lands through agricultural practices, particularly due to chemical fertilizers, pesticides, livestock manures and compost, sewage-sludge based biosolids, and irrigation; (2) factors affecting the bioavailability of HM elements in the soil solution, and their absorption, translocation, and bioaccumulation in crop plants; (3) mechanisms by which HM elements directly interfere with the physiological, biochemical, and molecular processes in plants with particular emphasis on the generation of oxidative stress, inhibition of photosynthetic phosphorylation, enzyme/protein inactivation, genetic modifications, and hormonal deregulation, and indirectly through inhibition of soil microbial growth, proliferation, and diversity; and (4) visual symptoms of highly toxic non-essential HM elements in plants with an emphasis on crop plants. Finally, suggestions and recommendations are made to minimize crop losses from suspected HM contamination in agricultural soils.

Keywords: heavy metals; arable lands; agricultural practices; soil binding models; action mechanisms; visual symptoms; crop production

1. Introduction

Metals including potentially toxic elements are inorganic elements containing atomic densities ($g.cm^{-3}$) several times higher than H_2O ($1.g.cm^{-3}$) and broadly classified into heavy and light metals, and semi-metals (Figure 1). Based on physical, physiological, and chemical properties, metals have been classified under several sub-groups, namely: transition metals: e.g., chromium (Cr), manganese (Mn), iron (Fe), cobalt (Co), nickel (Ni), copper (Cu), and molybdenum (Mo); post-transition metals: e.g., aluminum (Al), zinc (Zn), cadmium (Cd), mercury (Hg), and lead (Pb); alkaline earth metals: e.g., calcium (Ca), magnesium (Mg), beryllium (Be), and barium (Ba); alkali metals: e.g., lithium (Li), sodium (Na), potassium (K), and cesium (Cs); and metalloids, which are also referred to as semi-metals because of their metallic and non-metallic properties: e.g., boron (B), silicon (Si), arsenic (As), and antimony (Sb) [1].

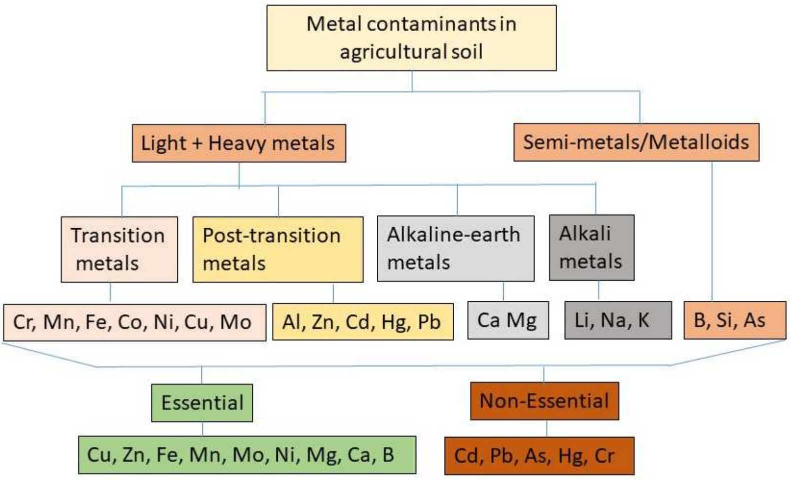

Figure 1. Classification of metallic and non-metallic elements, frequently found in agricultural soils. Mg (magnesium), Ca (calcium), Fe (iron), B (boron), Mn (manganese), Zn (zinc), Mo (molybdenum), Cu (copper), Pb (lead), Ni (nickel), Cr (chromium), As (arsenic), Hg (mercury), Cd (cadmium), Al (aluminum), Li (lithium), K (potassium), Na (sodium), Si (silicon).

Heavy metals and metalloids (HMs) are environmental pollutants. They are also agricultural soil contaminants because if present at elevated levels in the soil, HMs can negatively impact crop health and productivity [2,3]. HMs are recalcitrant to degradation, and if not taken up by plants or removed by leaching, they can accumulate in the soil and persist for long periods [4–6]. The elements that are frequently found to contaminate agricultural soils and cause toxic effects at elevated levels on plants include Cd, Pb, Cr, As, Hg, Ni, Cu and Zn [4,7]. Among them, Cd, Pb, As, Hg, and Cr are highly toxic and detrimental to plant health at almost all levels of contamination [8–10].

Several elements are classified as essential mineral nutrients for plant growth and productivity (Figure 1). Examples include Cu, Zn, Fe, Mn, Mo, Ni, Mg, Ca, and B. At relatively low concentrations, these elements can enhance specific cellular functions in plants including ion homeostasis, pigment biosynthesis, photosynthesis, respiration, enzyme activities, gene regulation, sugar metabolism, nitrogen fixation etc. [3,8,11]. However, when accumulated at concentrations above optimum, these same essential elements can adversely affect plant growth, development, and reproduction [2,3]. Conversely, if the concentration falls below certain threshold levels, they also produce mineral deficiency symptoms in plants [11].

HM contamination in agricultural soil is a global issue. The problem is more prominent in many developing countries partly because of rapid urbanization and industrialization, and perhaps partly due to lack of proper awareness about the toxic consequences of these elements not only to human health but also to crop health [12–16]. This review concentrates on the adverse effects of HMs on crop health.

2. Sources of HM contamination in arable lands

Agricultural soil is an important non-renewable natural resource. It can be contaminated with toxic HM elements such as Cd, Pb, Cr, As, Hg, Cu, Ni, Zn, Al, and several others due to natural causes as well as anthropogenic activities. Natural causes include, among many others, weathering of metal-bearing rocks by rainwater and atmospheric deposition. Anthropogenic activities include industrial activities (e.g., mining, leather tanning, textile, and petrol-chemical), disposal of metal containing wastes, vehicle exhausts, and agricultural practices [4,15,17–20]. However, irrespective of the source of contamination, continued addition of HMs to arable lands can result in soils that can be too toxic to support plant growth and productivity. The following subsections review primarily the contamination of HMs in farmlands through suspected agricultural practices as outlined in Figure 2.

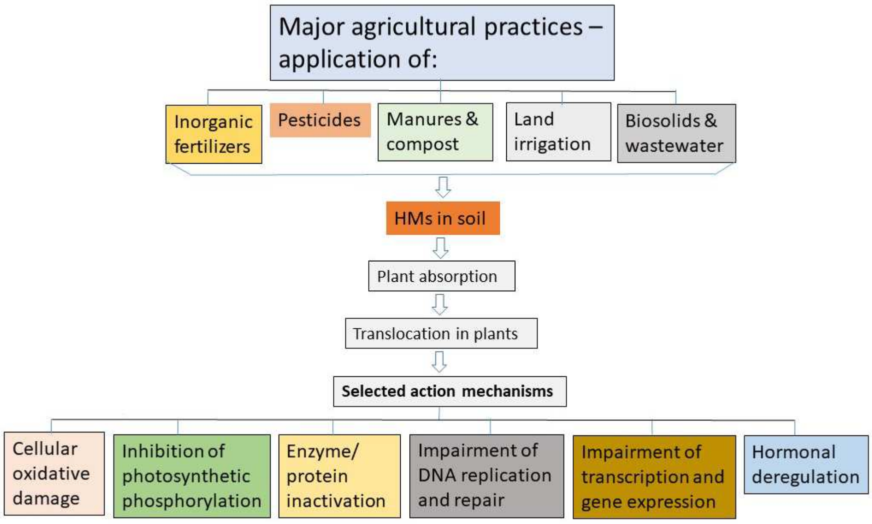

Figure 2. A flow chart showing the contamination of HMs in farmlands through agricultural practices, their absorption and translocation in crop plants, and the key mechanisms of action in plants.

2.1. *Application of chemical fertilizers*

Chemical fertilizers, particularly inorganic fertilizers, are a crucial input for crop production. Consequently, large quantities of inorganic fertilizers including nitrogen (N), phosphorus (P), potassium (K), and compound/mixed fertilizers are routinely added to agricultural lands to supply adequate quantities of these macronutrients. For instance, it was estimated that in 2019, more than 220 million tons of commercial fertilizers and liming materials were applied worldwide mostly to agricultural fields [21].

Among these fertilizers, P-fertilizers contain the highest level of HM contaminants [4,22–24]. For example, superphosphate fertilizers can contain Cd, Co, Cu, Pb, Zn, Cr and Ni as contaminants. In a study that assessed soil with and without P-fertilizer amendments, the concentration of Zn was higher not only in the amended soil but also in the plants grown in that soil [25]. Cadmium content in the soil has been shown to increase persistently due to application of P-fertilizers [12,23,26]. Cadmium is extremely toxic to plants because of its high solubility and mobility in soil solution. The concentration of Cd present as an impurity in several P-fertilizers evaluated in a study is shown in Table 1.

Table 1. Cadmium concentration in several phosphate fertilizers. Source: [27].

Fertilizers	Cadmium content (mg Kg^{-1})	
	Based on product	Based on P content
Complete fertilizer	23–29	418–527
Single superphosphate	16–26	186–302
Superphosphate	13–34	151–395
Rock phosphate	7.2–47	54–303
High analysis fertilizer	<0.6–5.6	15–118
Double superphosphate	<0.6–12	<3.6–72
Triple superphosphate	0.8–7.0	24–35
Mono-ammonium phosphate	1.8–8.1	12–37
Di-ammonium phosphate	4.3–6.6	22–28

In addition to P-fertilizers, copper sulphate, iron sulphate, and zinc sulphate fertilizers can also contain HM contaminants including Pb [22,27,28]. A study reported from greenhouse experiments that repeated application of chemical fertilizers significantly increased the accumulation of several

HM elements in the soil (Table 2). Sources of HM contamination in fertilizers include the raw materials used in the manufacture of inorganic fertilizers. For instance, phosphate-rock, also known as phosphorite is utilized in the production of P-fertilizers [29,30]. Over 90% of potash extracted from mines is used in the manufacture of K-fertilizer [31]. Based on the level of HM impurities, chemical fertilizers can be ranked as follows: P-fertilizers ≥ compound fertilizers> K-fertilizers> N-fertilizer [32,33].

Table 2. Heavy metal concentrations in greenhouse soil because of repeated application of inorganic fertilizers. Source: [24].

Elements	MAX	MIN	Fold difference
	mg Kg^{-1} soil		
Cadmium	0.65	0.06	10.8
Copper	171.5	21.0	8.2
Nickel	36.9	28.7	1.3
Lead	38.0	20.5	1.9
Zinc	433	71.9	6

2.2. Pesticide application

Pesticides play an important role in global agriculture. It has been estimated that without pesticides the world's food production can be reduced close to ~40% [34]. Another study estimated a 78% loss of fruit production, 54% loss of vegetable production, and 32% loss of cereal production without pesticide use [35]. Pesticides such as insecticides, fungicides, rodenticides, nematicides, and herbicides are composed of either organic or inorganic compounds that are toxic to the targeted organisms. Analysis of these compounds shows that some of them contain HM elements either as active ingredients (Table 3) or as impurities in the formulations (Table 4).

Several fungicides and insecticides extensively used in the past in agricultural lands were shown to contain significant concentrations of HM elements in their active ingredients. Examples include Cu containing fungicides such as copper sulphate (Bordeaux mixture also referred to as Bordo® mix) and copper oxychloride; Pb containing insecticide such as lead arsenate; and Cu containing insecticide such as copper acetoarsenite. The commonly found HM elements in the active ingredients of pesticide products include Cu, As, Pb, Hg, Cr, Zn, Al, Li, Ba, B, and Ti (titanium) [36,37].

Table 3. Pesticides containing different HM elements in their active ingredients. Sources: [36,37].

Chemical name	Formula	HM elements
Insecticides		
Aluminium phosphide	AlP	Al
Aluminium silicate	$Al_2Si_2O_7$	Al
Arsenic acid	H_3AsO_4	As
Copper acetoarsenite	$C_4H_6As_6Cu_4O_{16}$	As, Cu
Copper oxide	Cu_2O	Cu
Copper carbonate	CH_2Cu_2O	Cu
Copper naphthenate	$C_{22}H_{14}CuO_4$	Cu
Lead arsenate	$AsHO_4Pb$	As, Pb
Lithium perfluorooctane sulfonate	$C_8F_{17}LiO_3S$	Li
Sodium meta-arsenite	$NaAsO_2$	As
Fungicide		
Copper oxide	CuO	Cu
Copper bis(3-phenylsalicylate)	$C_{26}H_{18}CuO_6$	Cu
Copper abietate	$C_4 0H_{58}CuO_4$	Cu
Copper acetate	$Cu_2(CH_3COO)_4$	Cu

Copper carbonate	CH_2Cu_2O	Cu
Copper chloride	$CuCl_2$	Cu
Copper hydroxide	H_2O_2Cu	Cu
Copper naphthenate	$C_{22}H_{14}CuO_4$	Cu
Copper oxychloride	$(ClCu_2H_3O_3)_2$	Cu
Copper sulphate	$CuSO_4\text{-}Ca(OH)_2$	Cu
Mercuric oxide	HgO	Hg
Mercurous chloride	Hg_2Cl_2	Hg
Methoxyethylmercury chloride	C_3H_7ClHgO	Hg
Methoxyethylmercury acetate	$C_5H_{1}0HgO_3$	Hg
Phenyl mercuric acetate	$C_8H_8O_2Hg$	Hg
Phenylmercury chloride	C_6H_5ClHg	Hg
Phenylmercury nitrate	$C_6H_5HgNO_3$	Hg
Sodium arsenite	$NaAsO_2$	As
Zinc borate	$ZnB_3O_4(OH)_3$	Zn, B
Zinc oxide	ZnO	Zn
Zineb	$C_4H_6N_2S_4Zn$	Zn
Herbicides		
Arsenic acid	H_3AsO_4	As
Calcium arsenate	$As_2Ca_3O_8$	As
Sodium arsenite	$NaAsO_2$	As
Cacodylic acid	$(CH_3)_2AsO(OH)$	As
Rodenticides		
Barium carbonate	$BaCO_3$	Ba
Zinc phosphide	Zn_3P_2	Zn
Thallium sulfate	Tl_2SO_4	Tl
Defoliants		
Sodium dichromate	$Na_2Cr_2O_7$	Cr
Zinc chloride	$ZnCl_2$	Zn
Mercuric chloride	$HgCl_2$	Hg

On the other hand, HM elements can also be present in pesticide products as impurities. For example, certain pesticide products used for pest control in Japan contained Cd, Hg, As, Cu, Zn, and Pb as contaminants [17]. Chemical analysis of several pesticides including 11 glyphosate-based herbicide formulations by utilizing inductively coupled plasma/optical emission spectrometry (ICP-OES) detected As, Cr, Co, Pb, and Ni as contaminants [38]. Similar analysis of several insecticides using ICP mass spectrometry detected Zn, Cu, Cr, Co, Pb and Tl (thallium) as contaminants [39]. It has been suggested that the HM elements contaminate pesticide products during manufacturing process, while some of them are intentionally added as nano pesticides for increased efficacy [38,40].

Table 4. Pesticide products containing HM elements as impurities.

Trade name	Technical name	Metal impurities (ppb)*
Insecticides		Defarge et al., [38]
Pyrinex®	Chorpyriphos	As (390), Cr (800), Ni (1200)
Polysect®	Acetamipride	Ni (50)
Fungicides		Defarge et al., [38]
Eyetak®	Prochloraze	As (200), Co (90), Cr (200), Ni (190), Pb (12)
Folpan®	Folpet	As (260), Cr (2000), Ni (1200)
Maronee®	Tebuconazole	As (90), Co (50), Cr (100)
Opus®	Epoxiconazole	Cr (90), Ni (60)
Pictor®	Boscalid	As (300), Co (275), Cr (1000), Ni (600)

Teldor®	Fenhexamid	As (575), Cr (800), Ni (800)
Herbicides		Defarge et al., [38]
R 3+®	Glyphosate based formulations	As (375), Co (50), Cr (175), Ni (20)
R Bioforce®		As (260), Cr (200), Ni (120)
R Express®		As (60)
R GT+®		As (450), Co (150), Cr (100), Ni (50), Pb (10)
R WeatherMax®		As (500), Cr (100), Ni (20), Pb (10)
Bayer GC®		As (75), Co (60), Cr, (110) Ni (20)
Clinic EV®		As (400), Co (90), Cr (150), Ni (20)
Glyfos®		As (200), Cr (1100), Ni (50), Pb (30)
Glyphogan®		As (320), Co (125, Cr (100), Ni (40)
Pavaprop-G®		Cr (110), N (190)
Radical Tech+®		As (270), Co (70), Cr (50), Ni (50)
Lonpar®	2,4-D	As (160), Cr (150), Ni (180)
Matin®	Isoproturon	As (100), Cr (100), Ni (30), Pb (25)
Starane®	Fluoroxypyr	As (75), Cr (250), Ni (100), Pb (100)
Insecticides		Alnuwaiser [39]
Sniper®	Fipronil	Zn (506), Cu (423), Cr (746), Co (275), Pb (88)
CyperCel®	Cypermethrin	Zn (2389), Cu (669), Cr (373), Co (18), Pb (807)
CyperSafe®	Cypermethrin	Zn (968), Cu (464), Cr (10), Co (6), Pb (119)
Scope 60®	Asaybrmthrin	Zn (527), Cu (539), Cr (437), Co (23), Pb (39)
Brodor®	Permethrin	Zn (10), Cr (16), Pb (186)
Clash®	Acephate + Buprofezin	Zn (1078), Cr (73), Co (39), Pb (1316)
Acefed®	Mithomail	Cu (19), Cr (48), Co (4), Pb (121)
Lanid®	-	Cu (128), Cr (60), Pb (98)
Probalt®	-	Cu (179), Cr (85), Co (25), Pb (46)
Nourcam®	-	-
Madar®	-	Zn (10), Cu (66), Cr (16), Co (10),
PifPaf®	-	Cu (110), Co (5), Thallium, Tl (19), Pb (12)
Paygon®	-	Zn (52), Tl (15), Pb (19)

*European Union (EU)/World Health Organization (WHO) prescribed permissible levels (ppb) in water: As (10), Cr (50), Ni (20/70), Pb (10), Co (NA).

2.3. Application of livestock manures and compost

Livestock manures are organic fertilizers composed predominantly of poultry, cattle, and pig manures. Application of these manures and the compost made from them to farmlands is a common practice in agricultural crop production. However, these manures and compost contain high concentrations of HM elements such as Cu, Zn, Cd, Ni, Cr, As, Pb, and Hg as contaminants [20,26,41,42]. A study conducted to determine the concentration of HM elements in different livestock and poultry manures is presented in Table 5. The major sources of contamination of HM elements in the manures include the minerals supplied with the commercial feeds [41,42]. For example, supplementation of animal feeds with growth-promoting organic arsenical products was practiced for many years [43]. Some studies confirmed that Zn, Cu, As, and Cd were artificially added to commercial feeds to promote animal growth and improve disease resistance [44,45]. However, animals cannot digest these HM elements and discharge them through manures [46]. Because HMs are non-degradable elements, they are also not broken down during the composting process [47]. Thus, long-term repeated applications of manures and compost can result in the buildup of HM elements to toxic levels in agricultural soil [48,49] and can affect crop health and productivity.

Table 5. A case study showing maximum (MAX) vs. minimum (MIN) concentration (mg Kg^{-1} dry weight) of HM elements in different livestock and poultry manures, and their fold differences (FD). Source: [42].

Source	Level	Zn	Cu	Pb	Cd	Cr	Hg	As	Ni
Pig	MAX	4639	1288	23	60	85	0.3	89	19
	MIN	100	73	0.3	0.04	3.5	0.0	0.01	4.7
	FD	**46**	**18**	**77**	**1500**	**24**	**-**	**8900**	**4.0**
Chicken	MAX	578	314	33	4.1	251	0.5	23	39
	MIN	166	18	3.0	0.03	4.0	0.02	0.05	5.2
	FD	**3.5**	**17**	**11**	**137**	**63**	**25**	**460**	**7.5**
Duck	MAX	682	199	41	2.5	64	0.07	6.8	16
	MIN	98	35	4.5	0.3	7.0	0.03	0.01	8.4
	FD	**7.0**	**5.7**	**9.1**	**8.3**	**9.1**	**2.3**	**680**	**1.9**
Poultry	MAX	682	314	41	4.1	251	0.5	23	39
	MIN	77	15	2.0	0.03	2.5	0.02	0.01	5.2
	FD	**8.9**	**21**	**21**	**137**	**100**	**25**	**2300**	**7.5**
Cattle	MAX	816	174	32	3.4	79	0.6	6.3	19
	MIN	49	12	1.6	0.04	0.8	0.02	0.01	4.2
	FD	**17**	**15**	**20**	**85**	**99**	**30**	**630**	**4.5**
Sheep	MAX	431	215	20	1.4	22	2.4	2.6	12
	MIN	42	8.4	1.7	0.3	8.0	0.2	0.6	1.2
	FD	**10**	**26**	**12**	**4.7**	**2.8**	**12**	**4.3**	**10**

2.4. Application of sewage-sludge based biosolids.

Sewage-sludge originated from municipal and industrial wastes can be highly contaminated with HM elements such as As, Cd, Cr, Cu, Pb, Hg, Ni, Mo, Zn, and others. Long term application of untreated sewage sludge in some developing countries has led to increased concentrations of HMs in the agricultural lands [14,20,50]. However, the biosolids generated from sewage-sludge processing plants can be typically low in HM contamination and can contain organic materials rich in nutrients, and be used as fertilizers [51,52]. When applied to arable lands, processed sewage-sludge can improve soil physical properties and crop productivity. Utilization of these byproducts for agricultural crop production is therefore a common practice in many countries. In the United States, about 3.0 million dry tons of biosolids are utilized annually for crop production [4]. The European community countries utilized >30% of processed sewage-sludge as a fertilizer in agricultural lands [53]. Australia incorporates over 175K tons of dry biosolid into agricultural soil [54]. In the United States, federal regulations limit concentrations of major elements (e.g., As, Cd, Cu, Pb, Hg, Ni, Se, and Zn) commonly found in biosolids for land application (Table 6), [52]. Although biosolids produced from sewage-sludge processing treatment are generally low in HM concentration, repeated applications of these products can result in the buildup of HM elements in agricultural soil and can negatively impact crop health and productivity.

Table 6. Regulatory limits for HM elements, commonly found in applied biosolids in the USA. Source: [55].

Elements	Maximum permissible level (mg Kg^{-1})	Cumulative loading rate (Kg ha^{-1})	Monthly average concentrations (mg Kg^{-1})	Annual loading rate (Kg ha^{-1})
As	75	41	41	2.0
Cd	85	39	39	1.9
Cr	3000	3000	1200	150
Cu	4300	1500	1500	75

Pb	840	300	300	15
Hg	57	17	17	0.9
Ni	420	420	420	21
Se	100	100	36	5.0
Zn	7500	2800	2800	140

2.5. Land Irrigation

Irrigation of agricultural lands with contaminated water from surface water bodies as well as groundwater sources is another route of HM contamination in agricultural soil. The above irrigation practices are more frequently followed in some developing countries [9,15,16,56,57]. A review of a large number of related articles published in a span of over two decades (1994 to 2019) that determined the HM contamination in surface water bodies throughout the world showed that the average content of Cr, Mn, Co, Ni, As and Cd exceeded the permissible limits as prescribed by WHO and United States EPA [9,20]. Studies conducted to determine HM concentration in irrigation water in several locations of the Gazipur district of Bangladesh, and the Gondar city of Ethiopia showed that in almost all of their tests the concentration of HMs exceeded the FAO (Food and Agriculture Organization) prescribed admissible levels (Table 7).

Table 7. HM concentrations in irrigation water reported in some studies as compared to FAO approved maximum permissible limits.

Elements	**Cr**	**Cu**	**Zn**	**As**	**Cd**	**Pb**	**Ni**	**References**
					mg L^{-1}			
Max level (FD)*	2.13 (21.3)	4.62 (23.1)	15.20 (7.6)	0.52 (5.2)	0.02 (2.0)	1.15 (0.2)	-	Ahmed et al., [16]
Max level (FD)	0.94 (9.4)	0.61 (3.1)	0.86 (0.4)	-	0.04 (4.0)	0.19 (0.04)	0.12 (0.6)	Berihun et al., [58]
FAO limit	**0.10**	**0.20**	**2.00**	**0.10**	**0.01**	**5.00**	**0.20**	

*Numbers in parentheses represent concentration FDs, calculated based on average concentration obtained divided by FAO limits.

The causes for HM contamination in surface water are both natural and anthropogenic, which include but are not limited to atmospheric deposition; geological and biological weathering; and discharge of agricultural, municipal, domestic, and industrial wastes. HM elements such as Pb, Ni, Cr, Cd, As, Hg, Zn, Cu, and others from diverse sources are transported to surface water bodies and irrigation canals through runoff, and to the underground aquifer through vertical leaching with percolating rainwater [16,59–61]. Thus, irrigation of croplands using HM contaminated water not only affects growth and productivity of crops [62] but can also threaten soil quality. It should however be noted that the extent of crop damage will depend on the pH of the irrigation water and redox potential and water solubility of the contaminated HM elements.

3. Factors affecting HM interactions with crop plants.

Several plant, soil, and metal related factors can influence HM interaction with crop plants [57,63–67]. The crop related factors include crop type (species, variety, genotype); growth stage and growth condition; metabolic activities; and uptake, translocation, and bioaccumulation capabilities. The major soil related factors include soil pH, organic matter (OM) content, cation exchange capacity (CEC), rhizosphere chemistry, and microbial activity. The minor soil related factors may include soil texture, hydration level, aeration (compactness), and temperature. The HM-related factors include speciation (organic vs. inorganic form), oxidation state, concentration, solubility, mobility, bioavailability, and interaction with soil particles and with the essential (e.g., Mg, Ca, Zn) or non-essential (e.g., Cd, Pb, Hg) ionic species.

3.1. Plant responses to HM toxicity

3.1.1. Plant type, growth stage, and growth conditions

The above features can influence HM interaction with crop plants. A few examples are cited below. Bean (*Phaseolus* spp.) plants exhibited tolerance to Cu toxicity at the early stages of growth as indicated by their primary photochemistry of photosynthesis [2,68]. The tolerance of alfalfa (*Medicago sativa*) plants to Cd, Cu and Zn toxicities was shown to be positively correlated with the plant age [69]. Tobacco (*Nicotiana tabacum*) plants accumulated relatively high concentrations of HMs in the leaves [70]. Among many vegetable species tested, specific species in the Brassicaceae family accumulated highest amounts of Cr, although Cr translocation from root to shoot was extremely limited in almost all species tested [71,72]. Investigation of several African vegetable species showed that the matembele (*Ipomoea batatas*) plants had the highest HM content followed by mchicha (*Amaranthus hybridus*), eggplant (*Solanum melongena*), and bamia (*Abelmoschus esculentus*) [65]. Root and shoot tissues of winter wheat (*Triticum aestivum*) tolerated high concentrations of Cd and can be used as an indicator for Cd contamination in agricultural soils [73]. Cadmium absorption capabilities of different rice varieties differed under similar growing conditions as some Japonica rice varieties had lower Cd concentration than most Indica varieties, and certain African upland rice varieties had even lower Cd absorption capabilities than the Japonica varieties [17]. Variability in HM absorption capabilities among different plant species or varieties may be caused by differences in morphological, physiological, anatomical, and genetic characteristics. Responses of several crop species to HM toxicity in the soil/nutrient culture as reported in some studies are shown in Table 8.

Table 8. Responses of crop plants to HM toxicity with respect to certain growth parameters.

Crop Species	HMs elements	Conc. (mg Kg^{-1} soil)	Height (cm)		Dry wt. (g)		Yield	Refs
			Shoot	Root	Shoot	Root	g/plot	
Helianthus annuus	Pb	0	53	34	4.3	2.5	-	Alaboudi et al., [74]*
		80	28	10	2.6	1.7	-	
		200	15	2	1.5	0.8	-	
	Cd	0	53	34	3.9	2.4	-	
		80	16	6	1.1	0.6	-	
		200	9	1.7	0.8	0.2	-	
Brassica Juncea	Cu	0	20	-	-	-	70	Cu [75]**
		100	15	-	-	-	50	
		200	13	-	-	-	33	
	Pb	0	20	-	-	-	70	
		100	13	-	-	-	35	
		200	11	-	-	-	31	
	Zn	0	20	-	-		70	
		300	17	-	-		64	
		500	16	-	-		44	
Oryza Sativa	Hg	mg L^{-1} nutrient solution			Pot^{-1}	Pot^{-1}		Du et al., [76]***
		0	-	-	0.52	0.19	-	
		0.5	-	-	0.28	0.17	-	
		1.0	-	-	0.22	0.12	-	
		2.5	-	-	0.17	0.08	-	

*Analytical grade HM salts dissolved in distilled water were mixed with air-dried loamy sand soil (pH >6.25; EC ~0.27 dSm−1; OM ~10.23%; HM status = under detection limits). **HMs in the form of $CuSO_4$, $Pb(NO_3)_2$, and

$ZnSO_4$ were mixed with alluvial soil (pH 6.15; OM ~2.44%; CEC 23.46 Cmol/kg; HM status (mg Kg−1 soil) = ~21.3; Pb ~57.2; Zn ~7.2). *** Different concentrations of $HgCl_2$ were mixed with nutrient solution (pH 5.5).

3.1.2. Plant metabolic activities

Plants have diverse mechanisms to prevent harmful effects of HMs including binding of HMs with the cell wall, transporting of HMs to vacuolar compartments, and synthesizing of metal binding proteins such as cysteine-rich metallothionein and phytochelatins. These proteins perform metal ion homeostasis, chelation, sequestration, and detoxification of excess HM elements in plant cells [77–80]. Reduced glutathione (GSH), the amino acid derivative of glutamic acid, cysteine and glycine has a strong affinity for HM elements such as Cd, Cu, Hg, Pb, Zn, Ni and As and acts as a ligand to chelate HMs to alleviate toxic effects on plants. Depending on their binding affinities with the GSH, HMs can be ranked as follows: Cd> Pb> Zn> Hg> As> Cu [81–83]. Some proteins belonging to mitogen-activated protein kinase (MAPK) are stimulated under Cu or Cd accumulation. These Cu or Cd-induced MAPKs enhance translation of transporters for HM sequestration and removal from plant cells [84]. Based on proteomic and other analyses, a study suggested that hemp plants can acclimate to high levels of Pb toxicity by enhancing photosynthesis (primary photochemistry), cellular respiration, and intercellular N and C assimilation; preventing unfolded protein aggregation and degrading misfolded proteins; and increasing transmembrane ATP transport [85]. Plants also release chemical messengers such as ethylene and jasmonic acid when grown in soil containing high levels of HMs that reduce HM toxicity in plants [86,87]. However, further research is needed to better understand how these signaling molecules interact with HM toxicity in plants.

3.1.3. Uptake, translocation, and bioaccumulation in plants

HMs enter plant roots via passive (apoplastic) or active (symplastic) movements [88,89]. However, the degree of phytotoxicity depends not only on root absorption but also on the translocation to different parts and accumulation to toxic levels in plants. For instance, a study showed that after 20 days of treatment, the translocation of Hg was <2% in the leaf and <4% in the shoot as compared to total quantity (μg g^{-1} DW) absorbed by roots of tomato seedlings [90]. Metal transporters play important roles in the uptake, translocation, and detoxification (by moving to vacuoles) of HMs in plants [91].

There are also antagonistic or synergistic interactions between HM elements during absorption or translocation in plants. For example, the presence of Hg in the growth medium significantly reduced As accumulation in the roots indicating the antagonistic effects of Hg against As absorption. However, the effect was synergistic when As was translocated to shoot particularly at higher Hg concentrations [76]. Cadmium uptake was reduced in rice plants when Fe plaque formed around roots indicating antagonistic effects of Fe on Cd uptake [92]. Another study showed that the Cr and Pb concentration in the locally grown vegetable species at the HM contaminated sites in Dhaka, Bangladesh was respectively, 10 and ~2 times higher than the FAO/WHO prescribed permissible limits in plants [93]. Based on the observations in several vegetable species, some studies suggested that differences in HM toxicity in plants can be attributed to their uptake and translocation differences [93,94].

Nonetheless, the overall phytotoxicity of HMs depends on, in addition to other factors, how plants carry out physiological functions such as phytostabilization (immobilization of HMs in the soil that can reduce bioavailability), rhizofiltration (adsorption of HMs with plant roots in the rhizosphere), phytoextraction (uptake and translocation of HMs in plants), phytoaccumulation (accumulation of HMs inside plants in active forms), and phytovolatilization (release of absorbed HMs in the atmosphere as volatile forms) [95–97]. However, the prevalence and bioavailability of HMs in the soils are basic requirements for phytotoxic effects in plants.

3.2. Occurrence and bioavailability of HMs

The occurrence of HMs in agricultural soils depends largely on the factors discussed in Section 2. The bioavailability and extractable concentration however appear to be predominantly controlled

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by the solubility of HMs in the soil solution and the OM content in the soil. Although there may be exceptions, in general the solubility of HMs in the soil can be positively correlated with [H$^+$] (acidity). For instance, the solubility of most HM ions is lower in the basic pH range whereas it is higher in the range of acidic pH [54,98,99]. It was shown that a one-unit decrease in pH value resulted in about two-fold more increase in the bioavailable concentration of certain elements such as Zn, Ni, Cd, Al, and Cu in the soil solution [100,101]. Agricultural soils can be expected to be more acidic particularly in the moderate to high rain fall areas due to loss of base forming ions (basic cations e.g., Ca^{2+}, Mg^{2+}, K$^+$, and Na$^+$) from the farmlands because of prolonged leaching. Furthermore, acidity can also buildup over time in the soil due to formation of inorganic acids such as phosphoric acid, sulfuric acid, and nitric acid in the soil due to oxidation of applied phosphorus, sulfur, and ammonium/nitrate fertilizers, respectively [102]. On the other hand, the OM content in the soil appears to have negative effect on HM uptake in plants perhaps due to chelation of HMs by forming metal-OM complexes [103,104]. The above suggests that HM bioavailability can be reduced in soil containing high OM content.

3.2.1. Hypothetical soil binding diagrams of HMs

While the exact mechanism(s) by which the soil pH and OMs control the bioavailability of HMs for plant uptake is (are) unclear, based on the above discussion we have formulated a hypothetical soil-binding model as displayed in Figure 3. It shows that in basic soils containing high OM content and low [H$^+$], most metal cations can be tightly attached to the negatively charged soil particles and become less available or unavailable for plant absorption (Figure 3A). On the other hand, in acidic soil containing high [H$^+$], these metal cations can either not able to compete with H$^+$ to bind with the soil particles or be released from soil particles in the presence high [H$^+$] (Figure 3C). These may consequently leave more HM elements in the soil solutions for plant absorption [105,106]. This diagrammatic model also suggests that soil OMs can play a crucial role in HM mobility and bioavailability for plant absorption. Since OMs make soil particles more negatively charged [107], most HM cations are attracted to, and perhaps bound tightly with the soil particles containing high OM (Figure 3A), becoming unavailable for plant absorption. On the contrary, soil particles with low OM content will have less net negative charges to bind with positively charged HM elements (Figure 3B), and this can result in the availability of some free HM ions in the soil solutions for plant absorption.

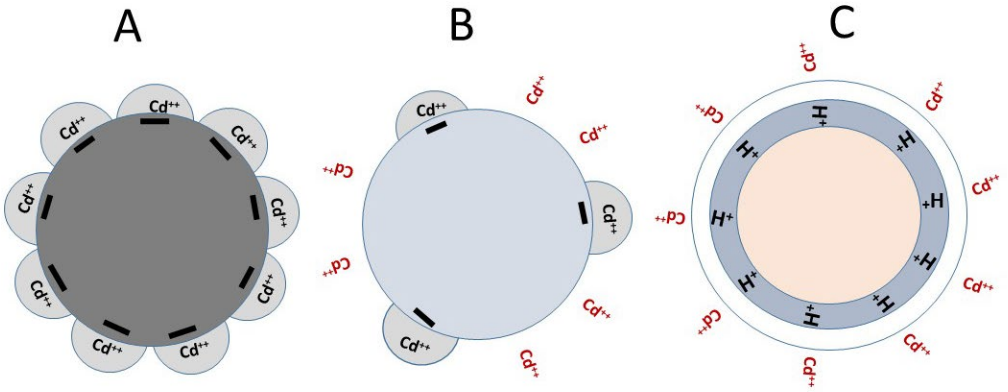

Figure 3. Hypothetical structural diagrams showing binding interactions of HM elements (e.g., Cd) with soil particles. A (basic soil): Cd^{2+} molecules held tightly with the soil the particle in the presence of high OM content by electrostatic forces (EFs); B (neutral soil): some Cd^{2+} molecules are available in free cationic form in the soil due to low OM content and low EFs; C (acidic soil): Cd^{2+} molecules are available in free cationic form in the soil containing high [H$^+$].

The hypothetical model presented above is consistent with previous studies which suggest that HMs can bind with organic molecules and become less biologically available for plant uptake

[103,108]. The above model also explains the reason why the bioavailability of HMs applied in the form of manure and compost is lower than that of HMs applied in salt forms [109]. A greenhouse study reported that application of chemical fertilizers increased the accumulation and bioavailability of Cu, Ni, Pb, and Zn in the greenhouse soil, and suggested that these HM elements were the contaminants of applied inorganic fertilizers [24]. Long-term field research also showed that the metal concentration in plants grown in soil amended with salt-forms of HMs was higher than that in plants amended with an equivalent quantity of HMs in organic or compost form [110].

From the above discussion, it appears that inorganic forms of HMs are readily available for plant uptake, whereas the organic and compost forms require microbial decomposition and conversion to inorganic forms for plant absorption. However, care should be practiced in adding processed sewage sludge based organic biosoilds in farmlands because excessive applications can cause soil structural modifications; deficiency of Zn, Mn, and Fe in plants due to phosphorus over-loading in the soil; and a buildup of HM elements such as Cu, Pb, and Zn to toxic levels for plant growth [111]. Further research would be needed to clarify the role of OMs and pH on the binding interaction of different HM elements with soil particles.

3.2.2. HM precipitation in the soil—effect of pH

Other lines of research suggest that in basic soils some HMs can be precipitated due to transformation into insoluble forms such as oxides, hydroxides, sulfides, sulfates, phosphates, silicates, carbonates etc. becoming biologically unavailable for plant absorption, whereas in the acidic soil, they can remain in free cationic forms in the soil solution and are biologically available for plant uptake [112–114]. The pH dependence of HM precipitation can vary among different elements because in most cases it is dependent on the oxidation states of the specific elements involved and the type reactions taking place in the soil solutions [112,115]. In general, an element containing higher oxidation states is more acidic than an element with lower oxidation states e.g., Fe^{3+} salts are more acidic than Fe^{2+} salts.

It appears that the above reports are consistent with the hypothetical diagrams presented in Figure 3, which also suggest that acidic soil pH can increase the bioavailability of certain metal cations, whereas basic pH reduces their availability for plant uptake. It has therefore been a common practice in agricultural farmlands with acidic soil to apply lime that elevates soil pH and perhaps alleviates metal toxicity to plants by converting them to insoluble forms as shown by the equation below [116].

$$CaCO_3 + H_2O \rightarrow Ca^{2+} + 2HCO_3- + 2OH^- \quad (1)$$

$$Al^{+3} + 3OH^- \rightarrow Al(OH)_3 \text{ (insoluble)} \quad (2)$$

$$H^+ + OH^- \rightarrow H_2O \quad (3)$$

However, it is important to keep in mind that over-liming can change soil physical, chemical, and biological properties, resulting in a situation where plants can suffer most notably from deficiencies of mineral nutrients such as Fe, Mn, Cu and Zn [117,118]. This is because the alkaline pH not only reduces uptake of toxic HM elements but also the uptake of essential mineral elements in plants. It is also worth mentioning that metal hydroxides including $Al(OH)_3$ can induce generation of ROS if sprayed to plants [119].

3.3. Rhizosphere chemistry and HM chelation

Plants' rhizosphere chemistry plays an important role in HM-plant interactions. For instance, under normal growing conditions, roots secrete organic molecules such as amino acids (e.g., methionine, lysine, and histidine) and organic acids (e.g., oxalic acid, citric acid, malic acid, tartaric acid, and succinic acid) that can bind with HMs and convert them to non-toxic forms [120,121]. It was shown that under Cd stress conditions, the total amount of organic acids secreted by the roots of Cd-tolerant rice varieties was ≥2 times higher than that of Cd-sensitive varieties [122]. Roots of a noncrop plant species grown in nutrient solutions containing Pb, Zn, Cu, and Cd salts secreted oxalic and malic acids in the media that made the plants more tolerant to the toxicity of these elements, suggesting chelation of HMs by these organic molecules [123]. The root-secreted organic molecules also provide nutrient resources to rhizosphere microbial populations to generate metabolites that can bind with the HMs and prevent them from root absorption [124]. For instance, a wide range of beneficial as well as pathogenic bacterial and fungal populations produce organic acids such as gluconic acid, oxalic acid, acetic acid, and malic acid as natural chelating agents for HM detoxification [125].

4. Key mechanisms of plant growth inhibition by HMs

Plants absorb HMs by roots from the soil solutions in the form of ions and transport them to various subcellular compartments through a diverse set of ion channels and transporter proteins such as HM ATPase, ATP binding cassette transporter, and cation diffusion facilitator [121]. If HMs exert detrimental effects on root growth, it will affect water balance and mineral nutrient uptake and translocation to the above ground shoot, causing negative impact on plant growth, biomass accumulation, and productivity.

On the other hand, if the concentration of HMs exceeds certain limits in the plants, they will affect cellular ionic homeostasis across membranes; structure and function of cell organelles (chloroplasts, mitochondria, nucleus, and vacuoles), and macromolecules (carbohydrates, lipids, proteins, and nucleic acids); and physiological, biochemical, and molecular processes in plants [11,79,80,126–131]. For instance, elevated levels of HMs have been shown to negatively affect chloroplast fine structure, chlorophyll a/b ratios, biosynthesis of photosynthetic machinery, pigment composition in grana and stroma membranes, and the activities of catalytic enzymes and non-catalytic proteins associated with various metabolic and developmental processes. The following sub-sections focus on key mechanisms of plant growth inhibition by HMs.

4.1. Generation of oxidative stress

Plants respond to toxic levels of HMs by overproduction of reactive oxygen species (ROS) such as superoxide radical (O^{2-}), hydrogen peroxide (H_2O_2), hydroxyl radical (OH^-), and singlet oxygen ($^1O_2$) at several sites including mitochondria, chloroplasts, peroxisomes, and at the extracellular side of the plasma membrane [132–134]. Although the redox active (Cr, Cu, Mn, Fe) and non-redox active (Cd, Ni, Hg, Zn, Al) elements generate ROS by different mechanisms, the generated ROS induce oxidative stress in plants leading to a variety of damages to cellular macromolecules including lipids, proteins, and nucleic acids. Some of the key consequences of cellular oxidative damage include lipid peroxidation; protein carbonylation, chain oxidation, misfolding, and aggregation; and breaks in DNA double-strands [128,130,135–142].

While in some cases, ROS generated in plants due to biotic or abiotic stresses including HMs can provide protection against certain fungal diseases [119,143], plants develop an antioxidant defense system involving ROS scavenging enzymes such as superoxide dismutase, catalase, peroxidases, and glutathione reductase that can dissipate ROS [144] and can protect plants from oxidative damage. However, certain HMs can disrupt the activity of some enzymes involved in defense responses [138,145,146]. Thus, the information generated above suggests that the contamination of elevated levels of HMs in agricultural soils and accumulation at toxic levels in crop plants can affect crop health and productivity not only by inducing oxidative stress but also by disrupting the antioxidant defense system in plants. However, further research is needed to clearly understand the specific relationship between HM stress and the antioxidant responses in plants.

4.2. Inhibition of photosynthetic phosphorylation

In the light-dependent reactions of photosynthesis, most HMs interfere with primary photochemistry, resulting in the inhibition of photosynthetic electron transport and phosphorylation. These effects were demonstrated in isolated chloroplasts, thylakoid membranes, and photosystem II

(PSII) submembrane fractions [128,147,148]. PSII mediated electron transport was suggested to be more affected by these elements compared to photosystem I (PSI) mediated electron transport. However, the actual mechanism of inhibition of PS II by HMs was unclear except that the oxygen-evolving complex (OEC) of PSII was suggested to be the probable target site [149]. By measuring the variable fluorescence of intact PSII membrane preparations in the presence of Pb^{2+} and other additives, it was suggested that the principal site of action of HMs was located on the water oxidizing side (WOS) of PSII [147]. The kinetics of variable fluorescence rise diminished as a function of Pb^{2+} concentration, suggesting that the electron transport on the WOS of PSII was inhibited by Pb^{2+}.

The above observation was further verified by immunoblotting with antibodies recognizing three extrinsic polypeptides of molecular masses, 16, 23, and 33 kDa associated with oxygen evolution of PSII. This study showed that the tested HM elements (Pb^{2+} and Zn^{2+}) selectively dissociated the above polypeptides from OEC [150]. It should be noted that these three polypeptides act as a shield to protect OEC from exogenous reductants in PSII submembrane preparations. Since depletion of these three extrinsic polypeptides from OEC by either HMs or detergent treatments can inactivate PSII [147,151–153], the generation of ATP, and the high-energy reducing agent, NADPH through noncyclic phosphorylation (to facilitate reduction of CO_2 to carbohydrate) is also expected to be inhibited (Figure 4). However, it is possible that in the absence of fully functional non-cyclic phosphorylation, plants can utilize PSI mediated cyclic electron flow to partially generate ATP to continue CO_2 fixation at a reduced rate [154]

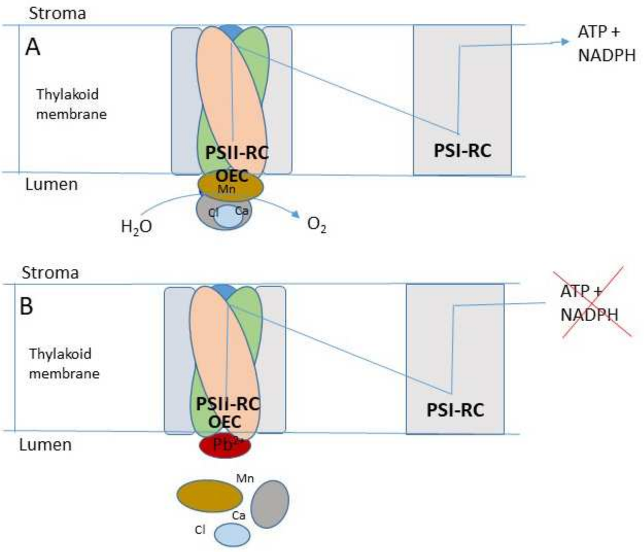

Figure 4. Diagrammatic drawing of a portion of thylakoid membrane showing stroma and lumen sides, locations of photosystem II (PSII) and photosystem I (PSI) reaction centers (RCs), and oxygen evolving complex (OEC). A: Generation of ATP and NADPH through photosynthetic electron transport in the absence of Pb^{2+}; B: Depletion of extrinsic polypeptide shield from OEC of PSII-RC and inhibition of phosphorylation and NADP reduction in the presence Pb^{2+}.

4.3. Inactivation of enzyme activities

4.3.1. Inactivation of soil enzyme activities

Enzymes in soil originate mostly from microorganisms and plants. The activities of these enzymes are a sensitive bioindicator of soil physical and chemical properties including nutrient cycling. These enzymes carry out many catalytic processes in the soil including decomposition of OMs to release mineral nutrients for plants. Some oxidoreductase enzymes such as dehydrogenases, nitrate reductase, catalase and peroxidases are involved in the degradation of many organic contaminants in the soil [155].

HMs inhibit the activities of many soil-associated enzymes involved in the transformation of carbon, nitrogen, phosphorus, and sulfur [156,157]. For example, the activities of catalase, urease, invertase, and phosphatase were inhibited in the soil upon addition of Pb, Zn, and Cu resulting in the reduction of growth and grain yield of barley [156]. Another study reported that the activity of seven enzymes was significantly reduced in response to soil contamination of Pb, Zn, Cd, Cu and As, and the order of inhibition of these enzymes was ranked as follows: arylsulfatase > dehydrogenase > β-glucosidase > urease > acid phosphatase > alkaline phosphatase > catalase [158]. This study further noted that clay-content and soil-depth negatively impacted the HM inhibition of soil enzyme activities. HM-induced inhibition of enzyme activities in the soil can occur due to multiple reasons such as formation of HM-substrate complexes, interaction of HMs with the enzyme-substrate complexes, binding of HMs with the active sites of the enzymes, denaturation of enzyme proteins, and interference with the growth of microbial populations involved in the synthesis of soil-borne enzymes [159,160].

4.3.2. Inactivation of plant enzyme activities

HMs interfere with cellular metabolic and developmental processes by inactivation of numerous enzymes and proteins in plants by binding to their active sites and functional groups such as carboxyl, amino, carbonyl, and sulfhydryl groups [130,146,161]. For instance, certain HMs inhibit the activities of enzymes involved in carbohydrate and phosphorus metabolism in plants (e.g., ribulose-1,5-biphosphate carboxylase, rubisco; phosphoenolpyruvate carboxylase; phosphoribulokinase; aldolase; fructose-6-phosphate kinase; fructose-1,6-bisphosphatase; NADP+- glyceraldehyde-3-phosphate dehydrogenase; carbonic anhydrase; and phosphatases) through conformational modifications by binding to their functional side chains [162–164]. Because of their strong affinity for -SH group, some HMs inhibit photosynthetic and water channel proteins by disrupting the disulfide bonds responsible for their structure and activity [8,79,165–167]. Some HMs inhibit the folding of nascent proteins causing aggregation in living cells. Nickel and Cd can make proteins non-functional by structural modifications such as unfolding which is corrected by plant chaperone system [168]. Bivalent Zn can inactivate rubisco activity by replacing bivalent Mg from the active site [169]. Lead and Zn can inactivate the water oxidizing enzyme of PSII by depleting Mn from the tetra-Mn-complex along with 33kDa extrinsic polypeptide [150]. Thus, HM induced enzyme inactivation and protein denaturation can cause multiple disturbances in crop plants affecting growth and crop productivity [141].

4.4. Genetic modifications

4.4.1. Effects on DNA metabolism

HMs are genotoxic but perhaps not mutagenic as there has been no report suggesting that HMs can induce gene mutations in plants, although Cr^{6+} is believed to be mutagenic to mammalian cells [170]. It is to be noted that all mutagenic substances are genotoxic, but not all genotoxic substances are mutagenic [171]. As discussed earlier, HMs can damage DNA molecules through generation of ROS in both plants and animals. They can also impair DNA replication and repair by inactivating enzymes involved in these processes [172]. For instance, As inhibits Poly-(ADP-ribose) polymerase-1 in humans, which is involved in the process of DNA-breakage repair caused by oxidative stress [173,174]. HMs such as Cd, Hg, and Pb can exert genotoxic effects on plants causing various types of lesions in DNA molecules. Elevated levels of Cd and Pb induce significant breakages in DNA double-strand, causing genome instability in faba bean (*Vicia faba*). Soil contaminated with Hg, Pb, Cu, Cd, and Zn caused increased levels of chromosomal abnormalities such as bridges, laggards, stickiness, and fragmentation in chickpea (*Cicer arietinum*). Certain HMs can damage DNA molecules by binding to phosphate backbones or nucleobases causing cleavage of DNA molecules. Mercury can form covalent bonds with DNA molecules resulting in the induction of sister chromatid exchange, decrease in mitotic index, and increase in the frequency of chromosomal aberrations [175,176].

4.4.2. Effects on gene expression

HMs regulate up or down expressions of many genes including the members of metal ATPase (*HMA2, HMA3, and HMA4*), metal transporter (*ZIPs, MTPs, NRAMPs, ABCs*), signal transduction (*MAPK*s), and metabolism-related families [177,178]. They can affect gene expression through inactivation of transcription factors (TFs) by replacing metallic components from metal-containing TFs. For example, Cd toxicity to Zn-finger TF was significantly reduced in the presence of sufficiently high level of Zn^{2+}, suggesting protective effect of Zn^{2+} against Cd toxicity to Zn finger TFs [179]. TFs of diverse families modulate plant responses to HM toxicity through positive or negative regulations of stress responsive genes [175,180]. For instance, barley plants overexpress dehydration related TFs to protect against toxic effects of Cd and Hg [10]. However, it was also shown that constitutive overexpression of some genes caused enhanced uptake of HMs in plants. Some genes expressed in response to metal exposure are encoded for proteins that perform membrane transport function for HM sequestration. Genetic modification of plants with such genes may be useful to enhance phytoremediation efforts in HM-contaminated soil. Plant cells also utilize various molecular mechanisms such as signal transduction, gene overexpression, RNA processing and transport, and post-translational modifications to counter the toxic effects of HMs and other stress factors in plants [10,181–183].

4.5. Hormonal deregulation

Among the plant hormones, auxins, cytokinins, gibberellins, abscisic acid (ABA), and ethylene are predominantly involved in growth regulations. However, ABA and ethylene also participate in stress responses along with defense hormones, salicylic acid (SA), jasmonic acids (JA), and brassinosteroids (BSs) [184,185]. Several investigations involving different crop species demonstrated that exogenous application of some hormones can partially alleviate the toxic effects of certain HMs on selected plant growth parameters, suggesting that HMs might exert negative impact on endogenous hormone levels in plants [186,187]. Several examples are cited below.

Exogenous application of kinetin (a cytokinin) was shown to reduce the inhibitory effects of Cd on several physiological parameters of pea plant, *Pisum sativum* (Table 9), suggesting that kinetin might have alleviated the toxic effect of Cd [188]. Exogenous GA_3 reduced the inhibitory effects of Cd and Pb on soluble protein contents in both broad bean (*Vicia faba*) and lupin (*Lupinus albus*), suggesting that GA_3 might have relieved the toxic effects of Cd and Pb on these vegetable species [189]. The auxin-induced alleviation of Cd toxicity in *Arabidopsis thaliana* was suggested to be due to increase in the level of hemicellulose content in the cell that fixed Cd within the cell wall and lessened Cd translocation from root to shoot [190]. Wheat plants treated with Cd exhibited a significant reduction in growth, pigment content, and the activities of antioxidant enzymes (superoxide dismutase, catalase, and peroxidase); however, pretreatment of these plants with indole acidic acid (IAA) or SA remarkably reduced Cd toxicity. These observations suggest that IAA and/or SA enhanced the antioxidant defense activities in Cd stressed wheat [191]. Treatment of tomato plants with BSs partially alleviated the toxic effect of Cd on growth and photosynthetic activity, which was suggested to be due to BSs-induced improvement of antioxidant activity in plants [192]. Based on these and similar observations in other studies, it can be assumed that the defense hormones (SA and BSs) can stimulate antioxidant defense system in plants in conjunction with other growth hormones (auxins and gibberellin) when exposed to HM toxicity [186,193,194].

Table 9. Partial alleviation of toxic effects of cadmium on some physiological growth parameters in pea plant (Pisum sativum) in the presence of a cytokinin hormone. Source: [188].

Physiological parameters*	Kinetin (μM)	Cadmium (μM)		
		0	25	50
Chl_a/Chl_b content (%)	0	100	73/72	48/44
	20	114/112	158/149	139/129
Photosynthesis rate (%)	0	100	88	42

	20	124	146	80
Soluble sugars content (%)	0	100	67	49
	20	180	226	249
Soluble proteins content (%)	0	100	119	133
	20	72	61	50
Amino acid content (%)	0	100	73	65
	20	132	179	200

* Control treatments as 100%.

In contrast, HMs can also influence the level of ABA, the negative growth regulator in plants. For example, numerous studies have shown that the level of endogenous ABA is elevated in the tissues of different plant species when exposed to the toxic levels of HMs such as Cd, Hg, Cu, Zn, Pb, and Ni [187,195]. Molecular analysis of plant tissues exposed to HMs showed strong expression of ABA biosynthesis genes and up-regulation of several ABA signaling genes [187]. Based on the above reports, it can be assumed that ABA perhaps coordinates protection against HM toxicity in plants. However, a study conducted utilizing ABA-deficient and ABA-sensitive mutants failed to establish such relationships at least at early stages of plant growth [196]. Thus, it is unclear as to how HMs and ABA interact with each other in plants although it has been established that ABA strongly reduced the phytotoxicity of HMs in plants [197,198]. Because ABA acts as a negative regulator of plant growth, it might be possible that ABA-induced inhibition of plant growth restricts HM translocation in plants.

While the exact mechanism of interactions between HMs and different growth and defense hormones is not fully understood, based on the reports presented above it can be assumed that plant hormones can modify HM toxicity in plants. Further research can help better establish the links between hormone signaling pathways and metal-binding ligands in plants.

4.6. Inhibition of soil microorganisms

Beneficial soil microorganisms including bacteria, fungi, actinomycetes and several others are indispensable components for crop productivity. They contribute to soil fertility and crop health in many different ways such as releasing nutrients from organic matters, recycling plant nutrients, and fixing atmospheric nitrogen to facilitate plant uptake; producing hormones, enzymes, and secondary metabolites to promote plant growth; degrading pesticides and other pollutants in the soil; controlling soil-borne pathogens by colonizing around plant roots to form physical barrier; producing antibiotics to inhibit pathogenic microbes; and improving soil physical structure to sustain agroecosystem [199,200].

Although at low concentrations, certain HMs can stimulate growth, at elevated levels they severely inhibit growth, proliferation, and diversity of soil microbial populations involved in beneficial activities stated above, thus indirectly affecting the crop health and productivity. Previous studies indicated that microorganisms are in general more sensitive to HM toxicity than other living organisms including plants growing in the same edaphic environment. However, the degree of toxicity of HMs to different microbial groups can also vary because it is dependent on inherent toxicity of the HM elements involved and their bioavailability in the soil [103,201–204]. Furthermore, some plant growth promoting bacterial species (e.g., Pseudomonas, Arthrobacter, Rhodococcus, Mesorhizobium, Agrobacterium, Bacillus, Azoarcus, Azospirillum, Azotobacter, Burkholderia, Klebsiella, Alcaligenes, Serratia, Rhizobium, and Enterobacter) are naturally tolerant to high concentrations of HMs for which they can be used in bioremediation of HM contaminated soils provided the soil conditions are favorable for their growth and proliferation [205,206].

HMs negatively affect soil microbial populations through enzyme/protein denaturation and destruction of cell membrane integrity. Many studies reported that HMs impair substrate utilization in enzyme-catalyzed reactions particularly during microbial respiration. For instance, when microbial growth media were amended with Zn, Cu, and Pb, the evolution of CO_2 was significantly reduced; however, when the media were supplied with adequate source of organic carbon, the negative effects on respiration was substantially reduced, confirming the effects on microbial respiration [203,207]. Despite some conflicting reports, the microbiological characteristics such as basal soil respiration; activities of dehydrogenase enzymes, which are inactive outside microbial cells; and quantification of phospholipid fatty acid (PLFA) molecule, which is decomposed upon microbial cell death can be used as sensitive indicators to approximately determine HM contamination in agricultural soils [208]. However, for precise determination of microbial diversity in HM contaminated soils, various molecular techniques including restriction fragment length polymorphism (RFLP) and sequence analysis of microbial genetic constituents such as 16S and 18SrRNA can be carried out [209].

5. Visual toxicity symptoms of HMs in plants

Numerous studies have shown that at elevated levels HMs induce oxidative stress, raise endogenous ABA levels, and interfere with many physiological and metabolic processes causing various growth abnormalities in plants including crop plants [3,187,210]. Because these abnormalities often resemble nutrient deficiencies as well as damages caused by diseases or pesticides [20,130,211–215], here we listed toxicity symptoms of non-essential HM elements that do not produce deficiency symptoms in plants (Table 10). Some of the common visible symptoms of these HM elements include chlorosis, inhibition of seed germination, stunting of root and shoot growth, reduction of biomass accumulation and yield, and occasional death of plants. Based on degree of plant toxicity, these HMs can be tentatively ranked as follows: Cd> As> Pb> Hg> Cr [216].

Table 10. Visual toxicity symptoms of HMs with no inherent symptoms of deficiency in plants.

Toxicity symptoms observed in some studies involving multiple plant/crop species	References for review
Cadmium (Cd^{2+}): solubility in water—high; mobility in soil colloids—high; bioavailability in soil—high; translocability in plants—high, toxicity in plants—highly lethal	
Chlorosis, wilting, leaf epinasty, stunting of plant growth.	Gill et al., [217]
Growth inhibition, leaf chlorosis and necrosis, and root browning.	López-Millán et al., [218]
Leaf rolling and chlorosis	DalCorso et al., [219]
Leaf chlorosis with green coloration around veins; leaf rolling, and growth stunting.	Sun et al., [220]
Reduction in seed germination, plant growth, biomass accumulation, and crop quality.	Rizwan et al., [221]
Chlorosis on newly expanded leaves, root growth inhibition.	Yamada et al., [216]
Growth stunting, chlorosis, root tip browning, and plant death.	Kumar et al., [20]
Stunting of growth, leaf chlorosis, reduction in fresh and dry biomass, plant death.	Ullah et al., [222]
Reduction in seed germination, shoot and root growth.	Chibuike and Obiora, [211]
Chlorosis, growth stunting, and necrosis.	Haider et al., [223]
Stunting of plant growth and blackening of roots.	Sharma and Dubey, [120]
Lead (Pb^{2+}): solubility in water—low; mobility in soil colloids—poor; bioavailability in soil—limited; translocability in plants—restricted; toxicity in plants—moderately lethal	
Inhibition of seed germination, early seedling growth, root and stem elongation, and leaf expansion.	Nagajyoti et al., [224]
Inhibition of seedling growth and secondary root growth.	Glinska et al., [225]
Inhibition of seed germination, seedling growth, root and stem elongation, and leaf expansion.	Asati et al., [130]
Inhibition of seed germination, seedling development, root elongation.	Tiwari and Lata, [8]
Stunting of shoot and root growth.	Kumar et al., [20]
Plant growth inhibition.	Xia et al., [85]

Inhibition of seed germination, root and shoot biomass, root elongation, and cell death.	Aslam et al., [226]
Inhibition of germination and seedling growth.	Gautam et al., [227]
Inhibition of seed germination, seedling height, number of roots per plant, and dry matter production.	Hossain et al., [228]
Arsenic (As^{3+} As^{5+}): solubility in water—high; mobility in soil colloids—high; bioavailability in soil—high; translocability in plants—high, toxicity in plants—lethal	
Reduction in leaf and root growth, wilting and violet coloration of leaves.	Abbas et al., [229]
Reduction in shoot and root length, and number of leaves per plant.	Imran et al., [230]
Reddening of tips, blades, margins, and midribs followed by yellowing of entire leaves.	Das et al., [231]
Shortening of plant height, premature shedding of leaves, and reduction in the number and size of nodules.	Huq et al., [232]
Reduction in leaf area, leaf fresh weight, fruit yield, seed germination, seedling height, and dry matter production; stunting of growth; chlorosis and wilting.	Asati et al., [130]
Reduction in seed germination, seedling height, leaf area, dry matter production, crop yield; chlorosis and wilting.	Chibuike and Obiora, [211]
Mercury (Hg^{2+}): solubility in water—low; mobility in soil colloids—low; bioavailability in soil—moderate; translocability in plants—limited, toxicity in plants—moderately lethal	
Abnormal germination, hypertrophy of root and coleoptile, inhibition of seedling growth.	Patra and Sharma, [233]
Reduction in germination, plant height, tiller and panicle production, biomass accumulation, and yield; chlorosis.	Chibuike and Obiora, [211]
Decrease in both root and shoot biomass.	Du et al., [76]
Inhibition of seed germination, shoot and root length, and fresh and dry matter production.	Gautam et al., [227]
Reduction in seed germination, embryo growth, primary root elongation.	Azevedo and Rodriguez, [146]
Inhibition of root and shoot biomass.	Cargnelutti et al., [234]
Inhibition of plant growth, biomass production, and leaf area.	Marrugo-Negrere et al., [235]
Inhibition of germination, seedling growth and development, biomass accumulation; leaf chlorosis and necrosis.	Singh et al., [236]
Chromium (Cr^{3+} Cr^{6+}): solubility in water—moderate; mobility in soil colloids—moderate; bioavailability in soil—moderate; translocability in plants—restricted; toxicity in plants—moderately lethal	
Inhibition of root and plant growth; leaf chlorosis.	Sharma et al., [186]
Inhibition of seed germination, root and shoot growth; reduction of plant biomass.	Asati et al., [130]
Inhibition of seed germination, seedling and plant growth.	Amin et al., [237]
Growth retardation, root discoloration.	Yamada et al., [216]
Chlorosis, necrosis; reduction in dry wight, nodulation, crop yield; inhibition of plant growth, root length	Samantaray et al., [238]
Inhibition of seed germination and seedling development and reduction of plant biomass and crop yield.	Stambulska et al., [239]
Inhibition of germination, root and shoot growth, dry matter production, and yield.	Shanker et al., [240]
Decrease in seed germination, reduction in growth, and yield.	Oliveira, [241]
Leaf interveinal chlorosis and root browning.	Nikolaou et al., [242]

6. Conclusions and perspectives

HMs are non-decomposable elements. Their contamination in agricultural soil is therefore a major threat to sustainable crop production in agriculture worldwide. The toxic effects of HMs on crop plants would become visible when their concentrations exceed threshold limits in the soil and tolerance levels inside crop plants. The bioavailability of HM elements toward crop uptake generally increases with acidic pH, lower OMs, and lower CEC of the soil. The HM induced reduction in plant growth and crop productivity can be attributed directly to, among others, the generation of oxidative stress; perturbation of ion homeostasis and water balance; decrease in mineral nutrient uptake and assimilation; reduction in photosynthetic rate; inhibition of enzyme activities; hormonal deregulations; and indirectly to the inhibition of beneficial microbial growth and proliferation in the soil.

However, plants have three major lines of defense against HM toxicity. The first line of defense involves prevention of HMs from entering the plants by forming extracellular complexes with root secreted organic molecules (e.g., amino acids, oxalic acid, citric acid, malic acid, tartaric acid, and succinic acid) or with root secreted secondary metabolites (e.g., flavonoids, phenolics, alkaloids, and other S- and N-containing compounds), or with microbial metabolites at the rhizosphere. The second line of defense includes chelation of HMs with carboxyl, hydroxyl, amino, and aldehyde groups of cellulose, hemicellulose, pectin, and proteins and compartmentalization inside cell vacuoles or osmotic adjustment of HMs by soluble sugars and proteins in plants. The third line of defense involves detoxification of generated ROS by antioxidant defense system in plants. Thus, if plants fail to properly execute the above defense barriers against HMs or if HMs could overcome these barriers, then the latter can greatly harm growth and productivity of plants including crop species.

To minimize crop injury from suspected HM buildup in agricultural soil, it is important that producers keep good records of application of pesticides, chemical fertilizers, livestock manures and associated composts, and sewage-sludge based biosoilds, as well as farmland irrigation. They should follow proper tillage practices (e.g., conservation tillage can increase soil acidity [243]) and crop rotation, maintain good OM levels in the soil, and adhere to judicial use of chemical fertilizers and pesticides in the farmlands. Since the growth of microbial populations is considered as one of the most sensitive indicators of monitoring metal toxicity determination, growers can test their soil samples by accredited commercial microbiological laboratories to determine microbial growth, diversity, and biomass. Because certain soil related factors, particularly pH, OM content, and CEC stated above can influence HM solubility and bioavailability for plant uptake, producers can also test their soil samples by certified chemical laboratories if crop injury is suspected from HM toxicity. However, prior to performing the above expensive tests, it is advisable to conduct a simple soil bioassay test utilizing HM sensitive crop cultivars following a similar procedure described in [215]. If HM contamination is confirmed from the afore-mentioned tests, it is important to follow proper remediation procedures.

For research-community engaged in molecular agriculture, it is important to develop HM tolerant crop cultivars by genetic manipulations of endogenous metal binding genes and the genes of antioxidant defense system of the target crop species. In addition, development of microbial biosensors for rapid detection of contaminated soil and the degree of contamination is also important for sustainable soil health and improved crop production. To facilitate research in the above fields, availability of funding is crucial.

Supplementary Materials: The following supporting information can be downloaded at: www.mdpi.com/xxx/s1, Table S1: Maximum allowable concentrations of HM elements in agricultural soil in several countries. Table S2: HM contamination in the soil of arable lands through suspected agricultural practices. Table S3: A summary of concentration fold differences of several HM elements in the edible plant parts of a number crop and vegetable species reported in some studies. Table S4: Maximum allowable limits of certain HM elements in food plants and plant-derived food commodities recommended by Codex Alimentarius commission. References [244–247] are cited in Supplementary Materials.

Author Contributions: For research articles with several authors, a short paragraph specifying their individual contributions must be provided. The following statements should be used “Conceptualization, X.X. and Y.Y.;

methodology, X.X.; software, X.X.; validation, X.X., Y.Y. and Z.Z.; formal analysis, X.X.; investigation, X.X.; resources, X.X.; data curation, X.X.; writing—original draft preparation, X.X.; writing—review and editing, X.X.; visualization, X.X.; supervision, X.X.; project administration, X.X.; funding acquisition, Y.Y. All authors have read and agreed to the published version of the manuscript." Please turn to the CRediT taxonomy for the term explanation. Authorship must be limited to those who have contributed substantially to the work reported.

Funding: Please add: "This research received no external funding" or "This research was funded by NAME OF FUNDER, grant number XXX" and "The APC was funded by XXX". Check carefully that the details given are accurate and use the standard spelling of funding agency names at https://search.crossref.org/funding. Any errors may affect your future funding.

Data Availability Statement: We encourage all authors of articles published in MDPI journals to share their research data. In this section, please provide details regarding where data supporting reported results can be found, including links to publicly archived datasets analyzed or generated during the study. Where no new data were created, or where data is unavailable due to privacy or ethical restrictions, a statement is still required. Suggested Data Availability Statements are available in section "MDPI Research Data Policies" at https://www.mdpi.com/ethics.

Acknowledgments: In this section, you can acknowledge any support given which is not covered by the author contribution or funding sections. This may include administrative and technical support, or donations in kind (e.g., materials used for experiments).

Conflicts of Interest: Authors declare no conflicts of interest.

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