Plant Archives Vol. 18 No. 2, 2018 pp. 1229-1238 **e-ISSN:2581-6063 (online), ISSN:0972-5210**

HEAVY METAL TOXICITY IN PLANTS: A REVIEW

Rubiya Syed[1], Dhriti Kapoor* and Arbeen Ahmad Bhat[1]

[1]Department of Botany, School of Bioengineering and Biosciences, Lovely Professional University, Jalandhar-144411 (Punjab) India

*Assistant Professor, Department of Botany, School of Bioengineering and Biosciences, Lovely Professional University, Jalandhar-144411 (Punjab) India

Abstract

Heavy metal toxicity has become a major consideration in today's world because of increased environmental pollution. Heavy metals are non-biodegradable and bio accumulative that frequently lead to deleterious biological effects. Plants require certain heavy metals for their growth and development but their excessive amounts can become toxic to plants by triggering the ROS generation such as ($O_{2}^{.-}$), ($OH^{.-}$), (H_2O_2) etc. that causes the oxidative stress by disturbing the equilibrium between pro-oxidant and antioxidant with in the plant cells and causes disorders like protein and lipid oxidation, DNA damage and denaturation of cell structure and membrane that finally results in the programmed cell death (PCD). To minimize ROS generation, there are enzymatic and nonenzymatic scavengers such as CAT, SOD, AsA, GSH etc that combats the metal stress in plants.

Key words: Heavy metals, reactive oxygen species, oxidative stress, antioxidative defense system.

Introduction

Plants frequently face different environmental stresses caused by biotic and abiotic factors, finally affects their growth and development (Xu *et al*., 2016). Biotic stress is caused by living organisms such as insects, nematodes, bacteria, fungi etc. (Gimenez *et al*., 2017). On the other hand, abiotic stress arise from high or low temperature, light, drought, salinity and heavy metals (fig 1) (Secchi *et al*., 2007). Among these stresses, heavy metal toxicity has become a major attention because of the enhanced environmental pollution. Since metals are non-decomposable, they frequently lead to deleterious biological effects (Jaleel *et al*., 2009). Plants life needs various heavy metals for their development but the extreme quantities of these heavy metals may be lethal to plant life. The plant is adversely affected by heavy metal stress, if the amount of metals inside the plant goes beyond normal level. The high concentration of metals can directly affect the plants such as inhibition of cytoplasmic enzymes and destruction to cell assemblies caused by oxidative stress. Heavy metals are significant environmental pollutants having toxic effects on ecological, evolutionary, nutritional and environmental reasons. They are the elements having higher atomic weight and density than that of water (Fergusson, 1990) and are toxic even at low concentration (Lenntch Water Treatment and Air Purification, 2004). Heavy metals include cobalt, nickel, copper, zinc, selenium, silver, antimony, thallium, arsenic, cadmium, mercury, lead and thallium (Fergusson, 1996). Arsenic, cadmium, chromium, lead, and mercury are treated as most important elements because they are having high degree of toxicity and are ranked as prior elements. These elements have adverse effects on human health and environment. There are both natural as well as anthropogenic sources of heavy metals. Mining and smelting operations and agricultural activities have contaminated the areas of World such as Japan and Indonesia. China is mostly affected by heavy metals like Cd, Cu and Zn (Herawati *et al*., 2000), whereas Cu, Cd, and Pb affected North Greece (Zanthopolous *et al*., 1999) Albania (Shallari *et al*., 1998) and Cr, Pb, Cu, Ni, Zn and Cd affected the areas of Australia (Smith, 1996).

Heavy metals are non-biodegradable and bio accumulative, which accumulates in ecological food chain

***Author for correspondence :** E-mail : dhriti405@gmail.com

by taking process from producer level and then through uptake at consumer level. In biological systems, heavy metals damages cellular organelles and components like mitochondria, lysosomes, DNA, proteins, carbohydrates, nuclei etc. which makes structural changes that may cause cell cycle variation, carcinogenesis or apoptosis (Chang *et al.*, 1996; Beyersmann and Hartwig, 2008).

Heavy metal toxicity prevents the plants to grow, plant functioning and acts as barrier to metabolic processes, causes disturbances to building blocks of protein structure that emerges from the formation of bonds between heavy metals and sulfhydryl groups (Hall, 2002), blocks functional groups of important cellular molecules (Hossain *et al.*, 2012), damages functionality of essential metals in biomolecules like pigments or enzymes (Ali *et al.*, 2013) and severely affect the integrity of plasma membrane (Farid *et al*., 2013), resulting in the controlling of vital activities in plants such as respiration, photosynthesis and enzymatic activities. The higher levels of heavy metals causes the increased production of reactive oxygen species (ROS), such as superoxide free radicals ($O_{2\cdot-}$), hydroxyl free radicles ($OH_{\cdot-}$) or non free radicles like hydrogen peroxide (H_2O_2), that causes the oxidative stress by disturbing the equilibrium between pro oxidant and antioxidant with in the plant cells, (Zengin and Munzuroglu, 2005, Hossain *et al*., 2012; Sytar *et al.,* 2013). This condition causes disorders like oxidation of proteins and lipids, leakage of ions, imbalance of redox and denaturation of cell structure and membrane that finally results in the programmed cell death (PCD) pathways (Nagajyoti *et al*., 2010; Flora *et al*., 2008).

According to Lushchak "Oxidative burst is a condition, when the concentration of reactive oxygen species (ROS are free radicals, very sensitive molecules and ions which have been originated from oxygen) are rapidly increased, results in the disturbances in cellular absorption, control and destroys the constituents of cell". Oxidative burst occurs when the cells are exposed to excess levels of ROS ($^1O_2$, $O_{2\bullet-}$, H_2O_2, •OH etc.) or when there is an antioxidant depletion. It is a difference between the formation of free radicals and the capability of body to nullify their harmful effects through neutralization by antioxidant (Halliwell and Gutteridge, 2006).

ROS species are generally generated under stress conditions and has high oxidizing activities that can attack biomolecules such as proteins, carbohydrates, lipids, nucleic acids etc. (Wojtaszek, 1997). ROS species are generated by different kinds of environmental stresses such as high light, low or high temperature, salinity, metal, drought, nutrient deficiency and pathogen attack. Plants

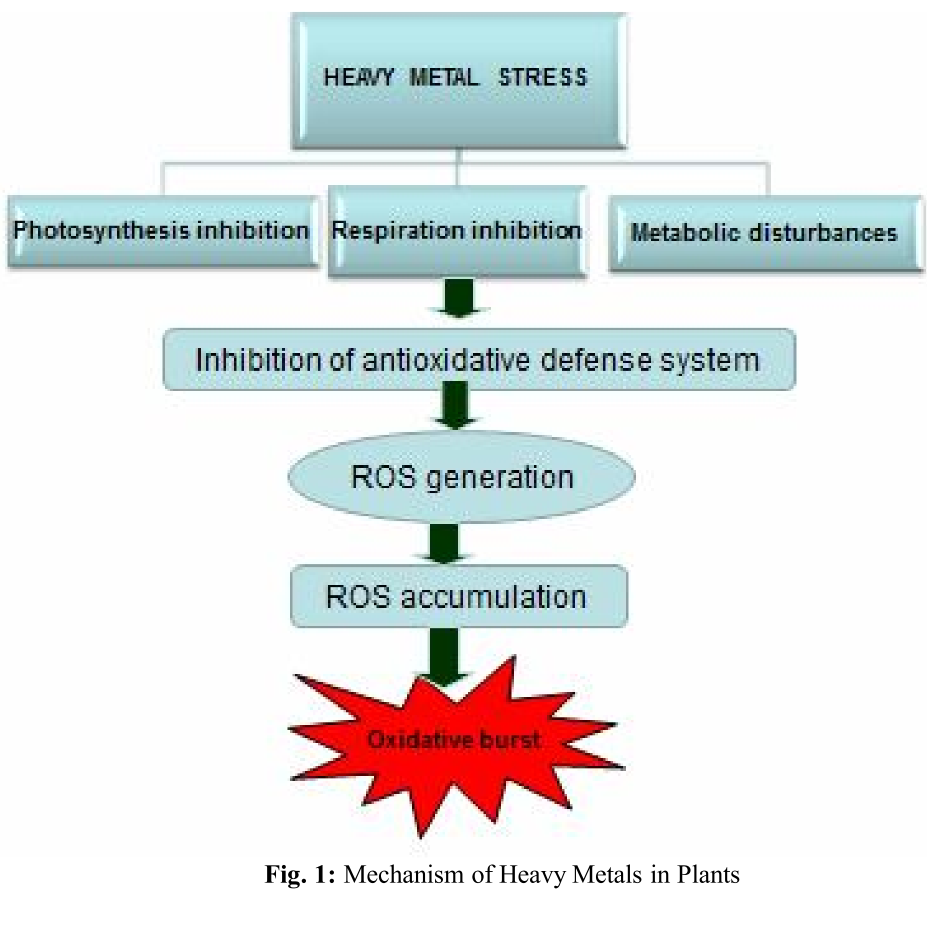

Fig. 1: Mechanism of Heavy Metals in Plants

consist of anti-oxidants and anti-oxidative enzymes that reduces or nullifies the effect of ROS. The imbalance between the ROS generation and the detoxification of these ROS by enzymatic and non-enzymatic reactions leading to oxidative stress which causes the DNA damage, damage to proteins and lipids and finally cell death. Inspite of destructive activities of ROS, they also act as a second messenger in different types of cellular processes which also includes the tolerance to environmental stresses (Desikan *et al*., 2001; Yan *et al*., 2007). Depending upon the equilibrium between ROS and detoxification, it will act as damaging or signaling molecule. Detoxification of excess ROS is attained by antioxidative system consisting of enzymatic and non enzymatic antioxidants (Noctor and Foyer, 1998). The enzymatic antioxidants are superoxide dismutase (SOD), catalase (CAT), guaiacol peroxidase (GPX), ascorbate peroxidase (APX), dehydroascorbate reductase (DHAR), monodehydroascorbate reductase (MDHAR) and glutathione reductase (GR), (Noctor and Foyer, 1998). The non enzymatic antioxidants includes glutathione (GSH), Ascorbate (AsA), carotenoids, tocopherols, phenolics etc. The increased activities of many enzymes of antioxidant defense system in plants have been reported by various workers that combat the oxidative stress induced by environmental stresses (Zaefyzadeh *et al*., 2009; Chen *et al*., 2011).

Effects of heavy metals on plants

Some heavy metal ions are essential micronutrients in a normal concentration but in higher concentrations they are highly poisonous to metabolic activities of plants.

On the basis of the physiochemical properties , bioactive metals are divided into redox-active metals such as Cr, Cu, Mn, and Fe and non-redox active metals such as Cd, Ni, Hg, Zn, and Al (Valko *et al*., 2005; Jozefczak, 2012). The redox metals undergoing through Haber-Weiss and Fenton reactions, can directly generate oxidative injury which leads in the production of ROS (Reactive Oxygen Species), resulting in cell homeostasis disruption, DNA damage, defragmentation of proteins, and damage to photosynthetic pigments, which may cause cell death (Schützendübel and Polle, 2002; Flora, 2009). On the other hand, non-redox active metals indirectly cause oxidative stress through various mechanisms including glutathione depletion, binding to sulfhydryl groups of proteins (Valko *et al*., 2005), inhibit antioxidative enzymes, or induce ROS-producing enzymes like NADPH oxidases (Bielen *et al*., 2013).

Heavy metal toxicity in plants is caused by three reasons:-

A: Production of methylglyoxal (MG) by auto-oxidation and ROS stimulation and by Fenton reaction or glyoxylase system and antioxidant defense system modification.

B: Heavy metal toxicity is also attributed by direct interaction of proteins because of having affinities for histidyl, carboxyl groups and for thiol which are responsible for making the heavy metals to target structural, catalytic, and transport sites of the cell.

C: From specific binding sites ,essential metal ions are displaced, resulting the function to collapse (Sharma and Dietz, 2009, Schutzendubel and Polle, 2002).

Heavy metal stress and plant response

Plants exposure to the toxic levels of heavy metals causes the physiological and metabolic alterations (Villers *et al*., 2011, Dubey, 2011). There are different sites of action for different heavy metals within the plant, however the most widespread evidence for the heavy metal toxicity is reduction of plant growth (Sharma and Dubey, 2007), also causes leaf chlorosis, necrosis, turgor loss, reduction in seed germination and a damaged photosynthetic apparatus, finally resulting in the plant death (Dolcorso *et al*., 2008; Dolcorso *et al.,* 2010). All these effects are responsible for molecular, ultrastructural, and bio-chemical changes in the plant cells and tissues (Gamalero *et al.,* 2009). HMs also affects homeostatic events such as water uptake, transport, transpiration and nutrient metabolism (Fodar, 2002; Poschenriedar and Barcelo, 2004) and also disturbs the uptake of Ca, Mg, K and P (Benavidis *et al*., 2005). High levels of the HMs also have direct effect on photosynthetic apparatus including thylakoids which decreases the rate of photosynthesis. HMs also creates a barrier in the release of proteins, lipids, and elemented components if thylakoid membranes, resulting in the damage to light-harvesting complexes and photosystem II (PS II) (Hsu and Kao, 2004; Bakor *et al*., 2006). HMs also causes reduction in Chl synthesis, which may be the cause of enzyme inhibition involved in the synthetic pathway (Boddi *et al* 1995; Shakya *et al.,* 2008). They also hinder carbon assimilation by inhibiting the enzyme which are involved in the fixation of CO_2 (Perfus-Barbeoch *et al*., 2002). It has also been observed that Cd induces the inhibition of respiration in Rice (*Oryzae sativa* L.*)* (Llamas *et al*., 2000). In response to As, the activities of starch phosphorylase, acid invertase, and sucrose synthase are increased where as the activities of alpha-amylase, ?-amylase and sucrose phosphate synthase is decreased in rice *(Oryzae sativa)* seedling (Jha and Dubhey, 2004).

Binding of HMs to cell nucleus are responsible for progenetic damage including DNA base modification,

Table 1: Effects of Heavy Metals on Different Plants.

Heavy Metals	**Plants**	**Adverse Effects**	**References**
Arsenic(As)	Rice *(Oryza sativa)*	Reduction in seed germination; decrease in seedling height; reduced leaf area and dry matter production.	Marin and Pezeshki, 1993
Cadmium(Cd)	Bladder campion (*Silene cucurbalus*)	Inhibits the nitrate reductase activity, interference with uptake, transport and use of several elements and affects photosynthesis.	Mathys *et al*., 1975.
Lead(Pb)	Rice*(Oryzae sativa)*	Affects vigor of seedling, chlorophyll, nitrogen and protein content, affects fresh and dry weight of in all varieties and affects more roots than shoots.	Kibria *et al*., 2010.
Arsenic(As)	Tomato *(Lycopersicon esculentum*)	Reduced fruit yield; decrease in leaf fresh weight	Barrachina *et al*., 1995
Chromium(Cr)	Tomato *(Lycopersicon esculentum*)	Decreases plant nutrients.	Shanker *et al*., 2003
Cadmium(Cd)	Oil seed rape (*Brassica napus L)*	Adverse effects on shoot growth and biomass	Li *et al*., 2009
Arsenic(As)	Canola*(Brassica napus)*	Stunted growth; chlorosis; wilting.	Cox *et al.* 1996
Cadmium(Cd)	Garlic(*Allium sativum*).	Reduces shoot length.	Jiang *et al*., 2007
Zinc(Zn)	Ryegrass(*Lolium perenne)*	Reduces the shoot growth and inhibits root growth.	Bonnet and veisseire, 2000
Mercury (Hg)	Rice (*Oryzae sativum*)	Decreases plant height,reduces tiller and panicle formation yield reduction.	Kibra, 2008
Arsenic (As)	Chickpea(*Cicer arietinum)*	Inhibits the growth of a chick pea plant.	Tu *et al*., 2004; Tu and Ma 2003; 2004; Srivastava *et al*., 2005.
Zinc(Zn)	(*Cyamopsis tetragonoloba*)	Excessive reduction in germination, chlorophyll, carote-noids, sugar, amino acids, and growth cluster of beans.	Manivasagaperumai *et al*., 2011.
Arsenic(As)	Maize (*Zea mays*).	Causes disruption of photosynthetic apparatus, inhibits the translocation to the shoots.	Baker and Rosenqvist, 2004
Cadmium(Cd)	Maize (*Zea mays),*	Reduces shoot and root growth.	Jiang *et al*., 2007
Mercury(Hg)	Tomato (*Lycopersicon esculentum*)	Reduction in germination percentage and flowering, reduce plant height and fruit weight and finally results in chloresis.	Shaker *et al*., 2011
Cromium(Cr)	Onion (*Allium cepa*)	Inhibits germination process and reduces plant biomass.	Nematshashi *et al.,* 2000
Cobalt(Co)	Radish (*Raphanus sativus)*	Reduces shoot and root length and total volume of leaf surface area, decreases chlorophyll content, reduces plant nutrient and antioxidant enzyme activity, and decreases sugar , amino acid and protein content.	Jaya kumar *et al*., 2008
Arsenic(As)	Maize (*Zea mays*)	Causes disruption of photosynthetic apparatus, inhibits the translocation to the shoots.	Bakerand and Rosenqvist, 2004
Nikle(Ni)	Winter rye grass (*Lolium perenne*)	Reduction in plant nutrient acquisition, decreases in shoot yield; chlorosios.	Sheoran *et al*.,1990
Iron(Fe)	*Nicotiana tabacum, Brassica napus, Glycine max, Hydrilla verticillata*.	Reduction in plant photosynthesis, yield, increases oxidative stress and ascorbate peroxidase activity.	Sinha *et al*., 1997
Arsenic(As)	Indian mustard(*Brassica juncea)*	Causes reduction in seed germination, root-shoot length, chlorophyll and protein content.	Chaturvedi, 2006.
Nikle(Ni)	Wheat species (*Tritium species*)	Reduces plant nutrient uptake.	Pandolifini *et al*., 1992; Barsukava & Gamzikova, 1991
Nikle(Ni)	Rice (*Oryzae sativa)*.	Inhibition of root growth.	Lin and .Kao, 2005
Arsenic(As)	Onion (*Allium cepa*).	Increases chlorophyll-a and chlorophyll-b content in onion leaf	Miteva & Merakchiyska, 2002
Arsenic(As)	Black gram (*Vigna mungo* L*)*	Reduction in length and dry weight of both shoots and roots.	Göhl *et al*., 1982

inter and intra-molecular crosslinking of proteins and DNA, rearrangement and de purination (Kasprzak *et al*., 1995). HMs alters the cell cycle and cell division by affecting the microtubule assembly-disassembly (Fusconi *et al*., 2006). *Arabidopsis* plants which are exposed to Cd show high mutation rate and malformed embryo (Dalcorso *et al*., 2010; Ernst *et al*., 2008). Ethylene level (gaseous hormone) is raised on the exposure of plants to the stressful conditions affecting the several plant responses including the senescence and stress (Deikman, 1997). In higher plants ethylene synthesis induced by Cu by means of lignification inhibits cell growth and increases cell wall rigidity (Enyedi *et al.,*1992) and can increase senescence (Maksymiec, 1997).

HM toxicity causes the accumulation of excess ROS inside the cell. The imbalance between the ROS generation and the detoxifications of these ROS by enzymatic and non-enzymatic reactions leading to oxidative stress which causes the DNA damage, damage to proteins and lipids and finally results in cell death

Mobality, Uptake, and Accumulation of Heavy Metals

Heavy metals accumulated in the environment are transported by air, water and finally gets deposited in soil and sediments where they could get deposited (Ozturk *et al*., 2008). However the process of bonding may take longer period of time. It has been observed that the bioavailable fraction of metal elements in the beginning of binding process is high in soil but it decreases gradually with the course of time (Martin and Kaplan, 1998). The bioavailability and the solubility of the metals mainly depends on the chemical properties of soil such as soil pH, cation exchange capacity, loading rate, soil texture, redox potential, clay content and organic matter (Verloo and Eeckhout, 1990). Soil pH is the most important parameter among the factors that are responsible for the accumulation of metals in plants (Deng *et al*., 2006). At higher soil pH, the elements of metal in soil decrease their bioavailability because they form low soluble compounds, whereas at lower soil pH, the metal bioavailability increases (Seregin and Ivanov, 2001).

Mechanism of toxicity and Carcinogenicity of various heavy metals

Arsenic

The toxicity of arsenic depends upon the degree of exposure, frequency, and duration, age, gender, biological species, genetic and nutritional factors, individual susceptibility (Abernathy *et al*., 2005) . Mostly the inorganic arsenic is responsible for the human toxicity. Penta-valent arsenic is 2-10 times less toxic than that of

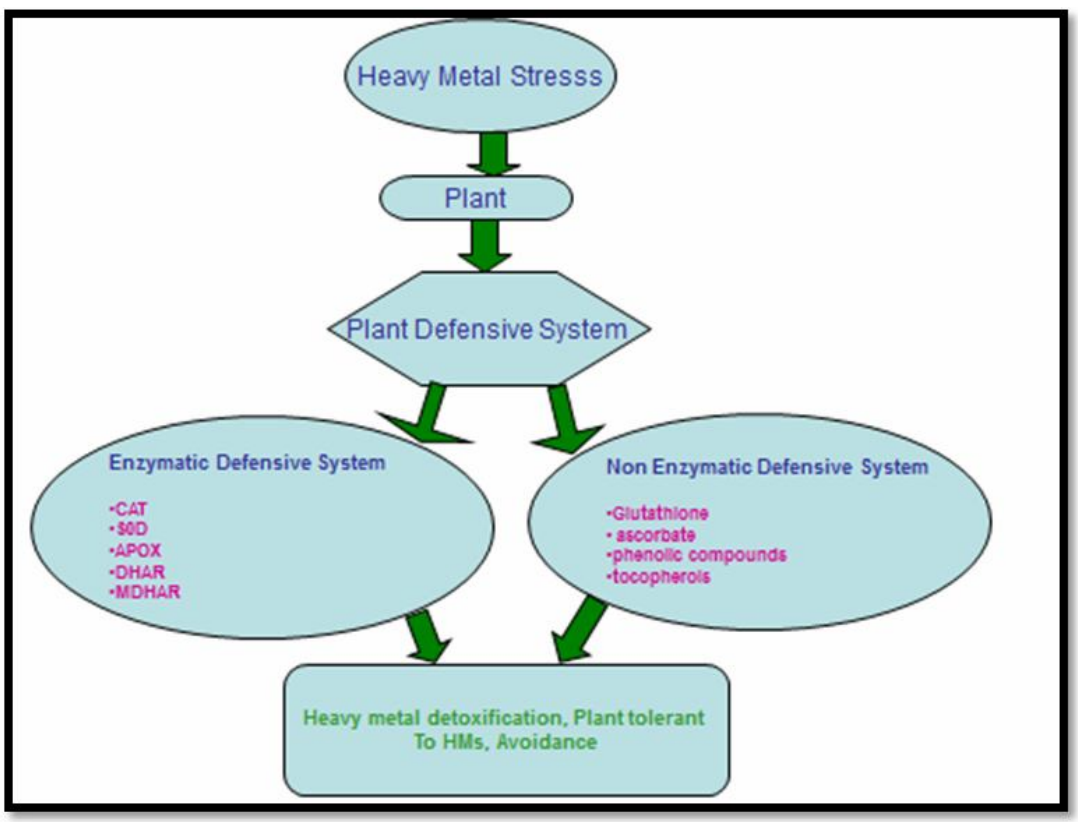

Fig.2: Mechanism of heavy metal tolerance

Tri-valent arsenite (Goyer, 2001) and As (III) has a capacity to inactivate over 200 enzymes. Arsenic causes uncoupling of oxidative phosphorylation and inhibits the mitochondrial enzymes through cellular respiration. It has been observed that the toxicity results from the interaction of Arsenic with sulfhydryl groups of proteins and enzymes and to replace the phosphorous in a variety of biochemical reactions (Wang and Rossman, 1996). Through non-enzymatic process, arsenic trioxide is methylated to monomethylarsonic acid (MMA), which in turn is enzymatically methylated to dimethyl arsenic acid (DMA) before excretion in the urine (Tchounwou. 2002, Hughes. 2002). Arsenic compounds have the ability to inhibit DNA repair and results in the inductionof chromosomal aberrations, exchange of sister chromatid and formation of micronuclei in human and in the rodent cells in the culture (Li JH *et al.*1982, Jha *et al.*1992, Hartmann and Speit, 1994) and in the exposed human cells (Patlolla and Tchounwou, 2005).

Induction of chromosomal aberrations, oxidative stress, repairing of DNA, alterations in the DNA methylation process, enhancement in the cell proliferation, alterations in the growth factors, promotion, p53 suppression and gene amplification (Miller *et al*., 2002). Presently, oxidative stress, chromosomal abberations and alterations in the growth factors have evidently found experimentally as well as in human tissues.

Cadmium

Severe exposure to Cr results in the adverse effects in the norepinephrine levels, serotonin levels and acetylcholine (Singhal *et al*.,1976), however the mechanism of Cd toxicity is not clearly understood. It has been guessed that Cr toxicity damages the cell through production of ROS (Stohs and Bagchi, 1995), which in turn damages DNA, hinders nucleic acid and protein synthesis (Mitra,1984). Several reports have shown that Cd has its effects on signal transduction pathways, which give rise to inositol polyphosphate formation, resulting in an increase in cytosolic free calcium levels in various cell levels (Thevenod and Jones, 1992), and calcium channels are blocked (Suszkiw *et al.* 1984, Dally and Hartwig, 1997). At the lower concentrations of Cadmium, it binds to proteins, decreases repairing of DNA (Abshire *et al*., 1996), protein degradation gets activated, causes up regulation of cytokinin and proto-oncogenes like c-fos, c-jun, and c-myc (Hwua and Yang, 1998), heme oxygenase, glutathione transferase, DNA polymerase beta (Landolph, 1994).

Chromium

Oxidation state and the solubility are the major factors that are responsible for the toxicity of Cr, Cr (VI) compounds is much more toxic than that of Cr (III) compounds (Connett and Wetterhahn, 1983; De Flora *et al.,* 1990). The ease of Cr (IV) by which it can pass easily through cell membranes and its successive intercellular reduction to reactive intermediates, may be related to the variation in toxicity. On the other hand Cr (III) is inadequately absorbed by any way; the toxicity of Cr is mainly due to Cr (IV) form. Cr (IV) can enter different types of cells and under physiological conditions, it can be reduced to hydrogen peroxide (H_2O_2), ascorbic acid, GSH and glutathione (GSH) and produce reactive intermediates including Cr(V), Cr(IV), thiylradicals, hydroxyl radicals and finally Cr(III). Any species among these causes disruption to cellular integrity and function by attacking DNA, proteins and membrane lipids (Mattia *et al.* 2004, Brien *et al*., 2003). It has been observed that the exposure of human beings to Cr(IV) leads to respiratory cancers (Costa,1997, Dayan and Paine, 2000), Oxidative damage results from genotoxic effects including chromosomal abnormalities (Wise *et al*., 2002, Wise *et al.,* 2004), breaks DNA strands (Xie *et al*., 2005).

Mercury

Mercury's molecular mechanism of toxicity is based on its biological characteristics and chemical activity (Valko *et al.*, 2005). Sulfhydryl reactivity mechanism is shown by mercury through oxidative stress. The site for the production of ROS in eukaryotes occurs in the mitochondria through normal metabolism (Shenkar *et al*., 2000). ROS produced by inorganic mercury causes damage in oxidative phosphorylation and electron transport at the ubiquinone-cytochrome b5 step (Palmeira and Madeira, 1997). Both organic and inorganic mercury through different mechanisms alter homeostasis. Mercury compounds induce increased levels of MDA in liver, kidney, lungs and tests of rats which are treated with $HgCl_2$ (Lash *et al*., 2007). Since ROS are generated through accumulation of mercury which causes the DNA damage. A process which can lead to the initation of carcinogenesis (Ogura et al 1996. Valko *et al*., 2006).

Mechanism of heavy metal detoxification

At the cellular level plants might have developed a potential mechanism of detoxification and thus give tolerance to heavy metal stress. There are some adaptive mechanisms evolved by tolerant plants includes immobilization, plasma membrane exclusion, synthesis of specific heavy metal transporters, chelation and sequestration of heavy metals by ligands (phytochelatins and metallothioneins), introduction of mechanism that compares the effect of ROS and MG (up regulation of anti oxidant and glyyoxalase system), stress proteins induction, proline biosynthesis and signaling molecules (Salysalic acid and nitric oxide) (Sharma and Dietz, 2009; Cobett, 2000; Clemins, 2006). The mechanism of heavy metal tolerance is shown in fig 2.

Conclusion

Metal stress is the major abiotic issue which reduces the crop productivity of agricultural crops by increasing environmental pollution. Excessive amounts of these metals may become toxic to plants by causing the oxidative burst. To minimize the ROS generation, there are enzymatic and non–enzymatic scavengers, which get activated in plants such as CAT, SOD, AsA, GSH etc. that combats the heavy metal stress by ameliorating the ROS.

References

Abernathy, C.O., D.J Thomas and R.L Calderon (2005). Health effects and risk assessment of arsenic. *American Society for Nutritional Sciences,* **133**: 1536S–1538S.

Abshire, M.K, D.E Devor, B.A Diwan, J.D Shaughness and Jr. M.P. Waalkes (1996). *In vitro* exposure to cadmium in rat L6 myoblasts can result in both enhancement and suppression of malignant progression *in vivo*. *Carcinogenesis,* **17**: 1349-1356.

Ali. H., E. Khan and M.A. Sajad (2013). Phytoremediation of heavy metals-concepts and applications. *Chemosphere,* **91**: 869–881.

Barrachina, A.C., F.B. Carbonell and J.M. Beneyto (1995). Arsenic uptake, distribution, and accumulation in tomato plants: effect of arsenite on plant growth and yield. *Journal of Plant Nutrition,* **18**: 1237– 1250.

Benavidis, M.P, S.M Gallego and M.L. Tomaro (2005). Cadmium Toxicity in Plants. *Brazilian Journal of Plant Physology,* **17**: 21-34.

Beyersmann, D. and A. Hartwig (2008). Carcinogenic metal compounds: recent insight into molecular and cellular mechanisms. *Arch Toxicol,* **82(8)**:493–512.

Bielen, A., T. Remans, J. Vangronsveld and A. Cuypers (2013). The influence of metal stress on the availability and redox state of ascorbate and possible interference with its cellular functions**.** *International Journal of Molecular Sciences,* **14**: 6382–6413.

Boddi, B., A.R. Oravecz and E. Lehoczki (1995). Effect of cadmium on organization and photoreduction of protochlorophyllide in dark-grown leaves and etioplast inner membrane preparations of wheat. *Photosynthetica,* **31**: 411–420.

Chang, L.M., L. Magos and T. Suzuki (1996). Toxicology of Metals. *Boca Raton. FL, USA***:** *CRC Press***.**

Chen, Q., M. Zhang and S. Shen (2010). Effect of salt on malondialdehyde and antioxidant enzymes in seedling roots of Jerusalem artichoke *(Helianthus tuberosus* L.*). Acta Physiologiae Plantarum,* **33**: 273–278.

Connett, P.H. and K.E Wetterhahn (1983). Metabolism of carcinogenic chromate by cellular constituents. *Struct Bonding,* **54**: 93-24.

Costa, M. (1997). Toxicity and carcinogenicity of Cr (VI) in animal models and humans. *Critical Reviews in Toxicology,* **27**: 431–442.

Cox, M.S, P.F Bell and J.L Kovar (1996). Different tolerance of canola to arsenic when grown hydroponically or in soil. *J. Plant Nutri*., **19**: 1599-1610.

Dalcorso, G., S. Farinati and A. Furini (2010). Regulatory networks of cadmium stress in plants. *Plant Signaling and Behavior,* **5:**1–5.

DalCorso G., S.Farinati, A.Maistri and A.Furini (2008). How plants cope with cadmium: staking all on metabolism and gene expression. *J. Integrative. Plant. Biol.,* **50**: 1268–1280.

Dally, H. and A. Hartwig (1997). Induction and repair inhibition of oxidative DNA damage by Nickel (II) and cadmium (II) in mammalian cells. *Carcinogenesis,* **18**: 1021-1026.

Dayan, A.D. and A.J. Paine (2001). Mechanisms of chromium toxicity, carcinogenicity and allergenicity: review of the literature from 1985 to 2000. *Hum. Exp. Toxicol,* **20**: 439-451.

De Flora, S., M. Bagnasco, D. Serra and P. Zanacchi (1990). Genotoxicity of chromium compounds: a review. *Mutat. Res.,* **238**: 99-172.

De Mattia, G., M.C Bravi, O. Laurenti, O. De Luca, A. Palmeri, A. Sabatucci, G. Mendico and A. Ghiselli (2004). Impairment of cell and plasma redox state in subjects professionally exposed to chromium. *Am. J. Ind. Med.,* **46**: 120-125.

Deikman, J. (1997). Molecular mechanisms of ethylene regulation of gene transcription. *Physiologia Plantarum,* **100**: 561–566.

Deng, H., Y. Z. ZH and M.H. Wong (2006). Lead and zinc accumulation and tolerance in populations of six wetland plants. *Environ. Pollut.,* **141**: 69–80.

Desikan, R., S. A.H. Mackerness, J.T. Hancock and S.J. Neill (2001). Regulation of the *Arabidopsis* transcriptome by oxidative stress. *Plant Physiology,* **127**: 159–172.

Dubey, R.S. (2011). Metal toxicity, oxidative stress and antioxidative defense system in plants. In Reactive Oxygen Species and Antioxidants in Higher Plants. 177–203. *CRC Press, Boca Raton, Fla, USA,* 177-203.

Duffus, J.H. (2002). Heavy metals-a meaningless term. *Pure Appl. Chem.,* **74(5)**: 793–807.

Enyedi, A.J., N. Yalpani, P. Silverman and I. Raskin (1992). Signal molecules in systemic plant resistance to pathogens and pests. *Cell,* **70**: 879–886.

Ernst, W.H.O., G.J. Krauss, J. A.C. Verkleij and D. Wesenberg (2008). Interaction of heavy metals with the sulphur metabolism in angiosperms from an ecological point of view. *Plant, Cell and Environment,* **31** 123– 143.

Farid, M., M.B. Shakoor, A. Ehsan, S. Ali, M. Zubair and M.S. Hanif (2013). Morphological, physiological and biochemical responses of different plant species to Cd stress**.** *International Journal of Chemical and Biochemical Sciences,* **3**: 53–60.

Fergusson, J.E. (1990). The Heavy Elements: Chemistry, Environmental Impact and Health Effects.Editor, Oxford: *Pergamon Press.*

Flora, S.J.S., M. Mittal and A. Mehta (2008). Heavy metal induced oxidative stress & its possible reversal by chelation therapy. *Indian Journal of Medical Research,* **128**: 501–523.

Fodar, F. (2002). Physiological responses of vascular plants to heavy metals. *In physiology and biochemistry of Metal Toxicity and Tolerance in plants. M.N.V Prasad and K. Strazalka,* ***Ed***, 149-177.

Fusconi, A., O. Repetto, E. Bona *et al.* (2006). Effects of cadmium on meristem activity and nucleus ploidy in roots of *Pisum sativum* L. cv. Frisson seedlings. *Environmental and Experimental Botany,* **58**: 253–260.

Gamalero, E., G. Lingua, G. Berta and B.R. Glick (2009). Beneficial role of plant growth promoting bacteria and arbuscular mycorrhizal fungi on plant responses to heavy metal stress. Canadian. *J. Microbiol.,* **55**: 501– 514.

Gimenez, E., M. Salinas and F.A Manzano (2018). Worldwide Research on Plant Defense against Biotic Stresses as Improvement for Sustainable Agriculture. *Sustainability,* **10**: 391-397.

Goyer, R.A. (2001). Toxic effects of metals. In: CD Klaassen (eds.): *Cassarett and Doull's Toxicology: The Basic Science of Poisons. McGraw-Hill Publisher. New York*. 811-867.

Hall, J.L. (2002). Cellular mechanisms for heavy metal detoxification and tolerance. *Journal of Experimental Botany,* **53**: 1–11.

Halliwell, B. and J.M.C. Gutteridge (2006). Free Radicals in Biology and Medicine, Ed 4. *Clarendon Press, Oxford.*

Hartmann, A. and G. Speit (1994). Comparative investigations of the genotoxic effects of metals in the single cell gel assay and the sister-chromatid exchange test. *Environ. Mol. Mutagen.,* **23**:299-305.

Herawati, N., S. Suzuki, K. Hayashi, I.F. Rivai and H. Koyoma (2000). Cadmium, copper and zinc levels in rice and soil of Japan, Indonesia and China by soil type. *Bull Environ. Contam Toxicol,* **64**: 33–39.

Hossain, M.A., P. Piyatida, J.A.T. da Silva and M. Fujita (2012). Molecular mechanism of heavy metal toxicity and tolerance in plants: central role of glutathione in detoxification of reactive oxygen species and methylglyoxal and in heavy metal chelation. *Journal of Botany Article,* Article ID, 872875, 37 pages.

Hwua, Y. and J. Yang (1998). Effect of 3-aminotriazole on anchorage independence and mutagenicity in cadmium- and lead-treated diploid human fibroblasts. *Carcinogenesis,* **19**: 881-888.

Jaleel, C.A., K. Jayakumar, Z.C. Xing and M.M. Azooz (2009). Antioxidant potentials protect *Vigna radiata* (L.) Wilczek plants from soil cobalt stress and improve growth and pigment composition. *Plant Omics,* **2**: 120–126.

Jayakumar, K., C.A Jaleel and P. Vijayarengan (2007). Changes in growth, biochemical constituents, and antioxidant potentials in radish (*Raphanus sativus* L.) under cobalt stress. *Turkish Journal of Biology,* **31**: 127–136.

Jha, A.B and R.S Dubey (2004). Carbohydrate metabolism in growing rice seedlings under arsenic toxicity. *J. Plant Physiol,* **161**: 867–872.

Jha, A.N., M. Noditi, R. Nilsson and A.T. Natarajan (1992). Genotoxic effects of sodium arsenite on human cells. *Mutat Res.,* **284**: 215-221.

Jiang, W., D. Liu and W. Hou (2001). Hyperaccumulation of cadm ium by roots, bulbs and shoots of garlic. *Bioresource Technology,* **76**: 9–13.

Jozefczak, M., T. Remans, J.Vangronsveld and A. Cuypers (2012). Glutathione is a key player in metal-induced oxidative stress defenses. *International Journal of Molecular Sciences,* **13**: 3145–3175.

Kasprzak, K.S. (1995). Possible role of oxidative damage in metalinduced carcinogenesis. *Cancer Investigation,* **13**: 411–430.

Kibria, M., M. Maniruzzaman, M. Islam and K. Osman (2010). Effects of soil applied lead on growth and partitioning of ion concentration in *Spinacea oleracea* L. tissues. *Soil Environ.,* **29**: 1-6.

Kirkham, M.B. (2006). Cadmium in plants on polluted soils: effects of soil factors, hyperaccumulation and amendments. *Geoderma,* **137**:19–32.

Landolph, J. (1994). Molecular mechanisms of transformation of CH_3/10T1/2 C1 8 mouse embryo cells and diploid human fibroblasts by carcinogenic metal compounds. *Environ Health Perspect,* **102**: 119-125.

Lash, L.H., D.A. Putt, S.E. Hueni, S.G. Payton and J. Zwicki (2007). Interactive toxicity of inorganic mercury and trichloroethylene in rat and human proximal tubules (Effects of apoptosis, necrosis, and glutathione status). *Toxicol Appl. Pharmacol,* **221**: 349-362.

Li. J.H. and T.C. Rossman (1989). Inhibition of DNA ligase activity by arsenite: *A possible mechanism of its Comutagenesis Mol. Toxicol,* **2**: 1-9.

Lin, Y.C. and C.H. Kao (2005). Nickel toxicity of rice seedlings: Cell wall peroxidase, lignin, and $NiSO_4$- inhibited root growth. *Crop, Environment Bioinformatics,* **2**: 131-136.

Llamas, A., C.I. Ullric and A. Sanz (2000). Cd^{2+} effects on transmembrane electrical potential difference, respiration and membrane permeability of rice (*Oryza sativa* L.) roots.

Plant and Soil, **219**: 21–28.

Maksymiec, W. (1997). Effect of copper on cellular processes in higher plants. *Photosynthetica,* **34**: 321–342.

Marin, A.R., S.R. Pezeshki, P.H. Masscheleyn and H.S. Choi (1993). Effect of dimethylarsinic acid (DMAA) on growth, tissue arsenic and photosynthesis of rice plants. *J. Plant Nutr*., **16**: 865- 880.

Martin, H.W. and D.I. Kaplan (1998). Temporal changes in cadmium, thallium and vanadium mobility in soil and phytoavailability under field conditions. *Water Air Soil Pollut.,* **101**:399–410.

Mathys, W. (1975). Enzymes of heavy metal-resistant and non-resistant populations of Silene cucubalus and their interactions with some heavy metals *in vitro* and *in vivo. Physiol. Plant.,* **33**: 161–165.

Miteva, E. and M. Merakchiyska (2002). Response of chloroplasts and photosynthetic mechanism of bean plants to excess arsenic in soil. *Bulg. J. Agric. Sci*., **8**: 151-156.

Mitra, R.S. (1984). Protein synthesis in *Escherichia coli* during recovery from exposure to low levels of Cd^{2+}. *Appl. Environ Microbiol,* **47**: 1012-1016.

Nagajyoti, P.C., K.D. Lee and T.V.M. Sreekanth (2010). Heavy metals, occurrence and toxicity for plants: A review. *Environmental Chemistry Letters,* **8**: 199–216.

Nematshahi, N., M. Lahouti and A. Ganjeali (2012). Accumulation of chromium and its effect on growth of (*Allium cepa* cv. Hybrid). *European Journal of Experimental Biology,* **2**: 969– 974.

Noctor, G. and C.H. Foyer (1998). Ascorbate and glutathione: keeping active oxygen under control. *Annual Review of Plant Biology,* **49**: 249–279.

O' Brien, T.J, S. Ceryak and S.R. Patiern (2003). Complexities of chromium carcinogenesis: role of cellular response, repair and recovery mechanisms. *Mutat. Res.,* **533**: 3-36.

Ozturk, M., E.Yucel, S. Gucel, S.Sakcali and A. Aksoy (2008). Plants as biomonitors of trace elements pollution in soil. *In: Prasad MNV (eds) Trace Elements: Environmental Contamination, Nutritional benefits and Health Implications,* **28**: 723–774.

Palmeira, C.M. and V.M.C. Madeira (1997). Mercuric chloride toxicity in rat liver mitochondria and isolated hepatocytes. *Environ. Toxicol Pharmacol,* **3**: 229-235.

Pandolfini, T., R. Gabbrielli and C. Comparini (1992). Nickel toxicity and peroxidase activity in seedlings of *Triticum aestivum* L.. *Plant, Cell and Environment,* **15**: 719–725.

Patlolla, A. and P.B. Tchounwou (2005). Cytogenetic evaluation of arsenic trioxide toxicity in Sprague-Dawley rats. *Mut. Res – Gen. Tox. Environ. Mutagen.,* **587**: 126-133.

Perfus-Barbeoch, L., N. Leonhardt, A.Vavasseur and C. Forestier (2002). Heavy metal toxicity: cadmium permeates through calcium channels and disturbs the plant water status. *Plant Journal,* **32**: 539–548.

Poschenriedar, C. and J. Barcelo (2004). Water relations in heavy metal stressed plants. *In Heavy* Metal Stressed Plants*, M.N.V Prasad, Ed,* 249-270.

Quan, R., R. Shang, M. Zhang, H. Zhao and J. Zhang (2004). Engineering of enhanced glycine betaine synthesis improves drought tolerance in maize. *Journal Plant Biotechnol,* **2**: 477-486.

Ramos, I., E. Esteban, J.J. Lucena and A. Garate (2002). Cadmium uptake and subcellular distribution in plants of *Lactuca* sp. Cd–Mn interaction. *Plant Sci.,* **162**:761-767.

Rellan-Alvarez, R., C. Ortega-Villasante, A. Alvarez-Fernández, F.F.D. Campo and L.E. Hernández (2006). Stress responses of *Zea mays* to cadmium and mercury. *Plant and Soil,* **279**: 41–50.

Schützendübel, A. and A. Polle (2002). Plant responses to abiotic stresses: heavy metal-induced oxidative stress and protection by mycorrhization. *The Journal of Experimental Botany,* **53**: 1351–1365.

Schutzendubel, A. and A. Polle (2002). Plant responses to abiotic stresses: heavy metal-induced oxidative stress and protection by mycorrhization. *J. Exp. Bot*., **53**: 1351–1365.

Secchi, F., C. Lovisolo and A. Schubert (2007). Expression of OePIP 2.1 aquaporin gene and water relations of Olea europaea twigs during drought stress and recovery. *Annals of Applied Biology,* **150**: 163-167.

Seregin, I.V. and V.B. Ivanov (2001). Physiological aspects of cadmium and lead toxic effects on higher plants. *Russian J. Plant Physiol,* **4**: 523–544.

Shakya, K., M.K. Chettri and T. Sawidis (2008). Impact of heavy metals (copper, zinc, and lead) on the chlorophyll content of some mosses. *Archives of Environmental Contamination and Toxicology,* **54**: 412–421.

Shallari, S., C.Schwartz, A. Hasko and J.L. Morel (1998). Heavy metals in soils and plants of serpentine and industrial sites of Albania. *Sci. Total Environ.,* **19(209)**:133–142.

Sharma, P. and R.S. Dubey (2007). Involvement of oxidative stress and role of antioxidative defense systemin growing rice seedlings exposed to toxic concentrations of aluminum. *Plant Cell. Reports*, **26**: 2027– 2038.

Sharma, S. and K.J. Dietz (2009). The relationship between metal toxicity and cellular redox imbalance. *Trends Plant Sci*., **14**: 43–50.

Shekar, C.H.C., D. Sammaiah, T. Shasthree and K.J. Reddy (2011). Effect of mercury on tomato growth and yield attributes. *International Journal of Pharma and Bio Sciences,* **2**: 358–364.

Shenker, B.J., T.LGuo and I.M. Shapiro (2000). Mercury-induced apoptosis in human lymphoid cells: Evidence that the apoptotic pathway is mercurial species dependent. *Environmental Research Section,* **84**: 89 – 99.

Singhal, R.L., Z.Merali and P.D Hrdina (1976). Aspects of the biochemical toxicology of cadmium. *Fed. Proc.,* **35**: 75-80.

Sinha, S., M. Guptha and P. Chandra (1997). Oxidative Stress induced by iron in *Hydrilla verticillata* (i.f.) Royle: response of antioxidants. *Ecotoxicol Environ Safe,* **38**: 286–291.

Smith, S.R. (1996). Agricultural recycling of sewage sludge and the environment. *CAB International, Wallingford, UK.*

Stohs, Bagchi (1995). Oxidative mechanisms in the toxicity of metal ions. *Free Radic Biol. Med.,* **18**: 321-336.

Suszkiw, J., G. Toth, M. Murawsky and G.P. Cooper (1984). Effects of Pb^{2+} and Cd^{2+} on acetylcholine release and Ca^{2+} movements in synaptosomes and subcellular fractions from rat brain and Torpedo electric organ. *Brain Res.,* **323**: 31-46.

Sytar, O., A. Kumar, D. Latowski, P. Kuczynska, K. Strza³ka, and M.N.V. Prasad (2013). Heavy metal-induced oxidative damage, defense reactions, and detoxification mechanisms in plants. *Acta Physiologiae Plantarum,* **35**: 985–999.

Th'evenod, F. and S.W. Jones (1992). Cadmium block of calcium current in frog sympathetic neurons. *Biophys J.,* **63**: 162-168.

Valko, M., C.J. Rhodes, J. Monocol and M. Izakovic-Mazur (2006). Free radicals, metals and antioxidants in oxidative stress-induced cancer. *Chemico-Biological Interactions,* **160**: 1-40.

Valko, M., H. Morris and M.T.D. Cronin (2005). Metals, Toxicity, and oxidative Stress. *Current Medicinal Chemistry,* **12**: 1161–1208.

Verloo, M. and M. Eeckhout(1990). Metal species transformations in soil: an analytical approach. *Int. J. Environ. Anal Chem.,* **39**:170–186.

Villiers, F., C. Ducrix and V. Hugouviex *et al.* (2011). Investigating the plant response to cadmium exposure by proteomic and metabolomic approaches. *Proteomics,* **11**:1650-1663.

Wang, M., J. Zou, X. Duan, W. Jiang and D. Liu (2007). Cadmium accumulation and its effects on metal uptake in maize (*Zea mays* L.). *Bioresource Technology,* **98**: 82–88.

Wang, Z. and T.G. Rossman (1996). The Toxicology of Metals. *CRC Press, Boca Raton,* **1** : 221-243.

Williams, D.E, J. Vlamis, A.H. Purkite and J.E. Corey (1980). Trace element accumulation movement and distribution in the soil profile from massive applications of sewage sludge. *Soil Sci.,* **1292**: 119–132.

Wise, J.P. Sr., S.S. Wise and J.E. Little (2002). The cytotoxicity and genotoxicity of particulate and soluble hexavalent chromium in human lung cells. *Mutat Res,* **517**: 221–229.

Wise, S.S., A.L. Holmes, M.E. Ketterer, W.J Hartsock, E. Fomchenko, S.P. Katsifis, W.D. Thompson and J.P. Wise (2004). Chromium is the proximate clastogenic species for lead chromate-induced clastogenicity in human bronchial cells. *Mutat Res.,* **560**: 79–89.

Wojtaszek, P. (1997). Oxidative burst: an early plant response to pathogen infection. *Biochemical Journal,* **322**: 681–692.

Xie, H., S.S. Wise, A.L. Holmes, B. Xu, T. Wakeman, S.C. Pelsue, N.P. Singh and J.P. Wise Sr. (2005). Carcinogenic lead chromate induces DNA double-strand breaks in human lung cells. *Mutat Res.,* **586**: 160–172.

Yan, J., N. Tsuichihara, T. Etoh and S. Iwai (2007). Reactive oxygen species and nitric oxide are involved in ABA inhibition of stomatal opening. *Plant, Cell and Environment,* **30**: 1320–1325.

Zaefyzadeh, M., R.A. Quliyev, S.M. Babayeva and M.A. Abbasov (2009). The effect of the interaction between genotypes and drought stress on the superoxide dismutase and chlorophyll content in durum wheat landraces. *Turkish Journal of Biology,* **33**: 1–7.

Zanthopolous, N., V. Antoniou and E. Nikolaidis (1999). Copper, zinc, cadmium and lead in sheep geazing in North Greece. *Bull Environ Contam Toxicol,* **62**:691–699.

Zengin, F. K. and O. Munzuroglu (2005). Effects of some heavy metals on content of chlorophyll, proline and some antioxidant chemicals in bean (*Phaseolus vulgaris* L.) seedlings. *Acta Biologica Cracoviensia Series Botanica,* **47**:157–164.