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**Arsenic Pollution: An Insight into its Effect in Plant Productivity and Human Health**

Srimoyee Koner1, Ranjana Pal1,\*, Siddhartha Dutta2,\*

1 Department of Life Sciences, Presidency University, Kolkata – 700073, India.

2 Department of Biotechnology, University of Engineering and Management, Action Area III, B/5, Newtown, Kolkata, West Bengal 700156, India.

\*Corresponding: [sid.dutta@gmail.com](mailto:sid.dutta@gmail.com), [ranjana.dbs@presiuniv.ac.in](mailto:ranjana.dbs@presiuniv.ac.in)

**Abstract**

Arsenic (As), a naturally occurring metalloid, has been a major concern to the environment due to its adverse effects on the plants and human. Arsenic uptake and accumulation in plants has not only impaired the plant processes leading to loss in growth and crop yield but also resulted in toxicity in human due to biomagnification. With decades of research on the effects of arsenic accumulation on plant growth and development and its consequences in human health, we briefly discuss the effects of As on plants and humans. In the first part of the review the principles of uptake of As by plant from soil are discussed. In the second part, the primary mechanism through which the As accumulation affect plant productivity are discussed. The last part describes the effect As has on different human organs. Our mini-review serves to guide the ongoing and future research on the effects As contamination.

**Keywords:** Arsenic, pollution, plants, human, uptake, growth, productivity, health.

**1.Introduction:**

The earth’s crust consists of arsenic (As) at an average concentration of ∼5 microgram per gram [1]. However, it gets concentrated in some regions of the world where it can act as an environmental contaminant. Its increased level in the environment has become a global concern due to its toxic effect on plant growth and human health [2-5]. In nature, arsenic (As) is found in combination with inorganic or organic substances to form many compounds [6]. Inorganic arsenic compounds are found in soil sediment and ground water [7]. They are natural or may be formed due to human activity such as mining, mineral debris, glass manufacture, computer chips, wood preservatives, alloying agents and arsenic based pesticides [6, 8, 9]. Fish and shellfish are the main source of organic arsenic compounds [2].

The toxic arsenic level is detrimental to plant growth and productivity as well as affect human and animal health. In plants, the arsenic accumulation leads to perturbation in morphological, biochemical and physiological processes such as root and shoot growth, germination, photosynthesis, carbohydrate metabolism and nitrogen assimilation and an increase in reactive oxygen species (ROS) leading to oxidative stress [10-15]. Due to the ubiquitous presence and its accumulation in edible parts of plants, it is further consumed by the organisms higher in food chain. This biomagnification and transfer of the arsenic through the food chain is one of the modes by which the human body gets contaminated with the heavy metal [6, 16]. Over 100 million people around world are exposed to arsenic in countries like India, Bangladesh, Taiwan, Chile and United States. People are mostly exposed to inorganic arsenic through drinking water and from various foods (in fewer amounts). Arsenic toxicity is due to its mutagenic, teratogenic and carcinogenic effects in human [17]. Usually, arsenic can cause symptoms like nausea, vomiting, diarrhea, dehydration, numbness or tingling of the extremities, muscle cramping, skin disorder, increased risk of diabetes, hypertension, peripheral neuropathy and several type of cancer [2, 18].

This mini-review aims to provide insight into the progresses in our understanding on the effects of the As in the context of plant growth and human health.

**2.Arsenic Uptake by Plants:**

Absorption by roots is the major route by which As is taken up by plants. Among the different oxidation state of As, trivalent arsenite As(III), pentavalent arsenate As(V) and methylated As [in the form of monomethylarsenic acid (MMAs) and dimethylarsenic acid (DMAs)] are the three predominant biologically relevant toxic form that are available to the plants. The availability of the different forms of As is primary dependent on the soil pH and temperature as well as microorganisms content of the soil [19, 20]. Although plants lack any dedicated As-specific uptake systems, they are taken up adventitiously by several types of transporters (Figure 1) [21-26].

*i)* *Arsenite uptake.* The As(III) is the most toxic arsenic species and is abundantly found in the anerobic environment including submerged soils. As(III) has been shown to be taken into root cells by the aquaporin (AQP) and members of major intrinsic proteins (MIP) [23, 24, 27]. Although aquaporins are small bidirectional channels that allow influx and efflux of water and small neutral molecules, they have been shown to be particularly relevant in the influx of As(III) in the root cells [27, 28]. Members of the nodulin 26-like intrinsic protein (NIP), a subfamily of plant MIP superfamily, have been shown to facilitate As(III) in the root cells [29]. Transgenic studies in *Arabidopsis thaliana* have identified at least six NIPs, NIP1;1, NIP1;2, NIP3;1, NIP5;1, NIP6;1 and NIP7;1, that are involved in As(III) uptake into the root [23, 24, 26, 30-32]. In rice (Oryza sativa), Lsi1 (also called NIP2;1), a silicon transporter, facilitates As(III) uptake into the root [22, 23]. In the roots, the expression of Lsi1 is high in the distal side of exodermis and endodermis which facilitates entry of As(III). In addition, members of plasma membrane intrinsic protein (PIPs), OsPIP2;4, OsPIP2;6 and OsPIP2;7, are also known to contribute to the As(III) influx in rice. Heterologous expression of OsPIP2;4, OsPIP2;6 and OsPIP2;7 in *Arabidopsis* resulted in increased influx of As(III) in response to short-term As(III) treatment [33].

*ii)* *Arsenate uptake.* As(V) is comparatively less toxic but most prevalent form of arsenic available in the aerobic soil and water. As the chemical structure of As(V) mimics the phosphate ions, it is adventitiously taken up by plant roots through the phosphate (Pi) transporters [34]. Till date numerous members of the Pi transporter 1 (Pht1) family have been identified which play active role in the As(V) uptake in plants (Figure 1). Initial studies in *Arabidopsis thaliana* led to identification of two Pi transporter, AtPht1;1 and AtPht1;4, which has high affinity for As(V) [35]. Several other members of the Pht1 family have been identified in *Arabidopsis*, such as AtPht1;5, AtPht1;7, AtPht1;8, and AtPht1;9 [36, 37]. The T-DNA mutants and overexpression analysis in rice led to identification of two Pi transporters, OsPht1;4 (OsPT4) and OsPht1;8, which are responsible for As(V) accumulation in root cells [25, 38, 39]. Recently, *Pteris vittate*, the first arsenic hyperaccumulator identified [40], was found to possess three Pht1 family Pi transporters, PvPht1;1, PvPht1;2 and PvPht1;3, that exhibit As(V) accumulation [41].

Figure 1. Schematic representation of As uptake and effects on diverse processes in plants. The white boxes in the lower panel contain the list of major transporters responsible for the As uptake by roots. The different colored boxes in the upper panel represents different effects of As toxicity on plants; growth and development are shown in blue, photosynthesis in brown, Pi associated cellular processes in grey, ROS homeostasis in yellow and metabolism in green.

*iii)* *Methylated arsenic uptake.* Methylated arsenic, MMAs and DMAs, exist widely in the environment. Although usage of herbicides and pesticides are responsible for the presence of methylated arsenic species in soil, it is the microorganisms that contribute to the major amount of the available methylated As in the soil [42-44]. At present, limited information is available on the variety of transporters that aids in methylated As uptake. The rate of methylated As absorbed by the roots is comparatively less efficient than that of the As(III) and As(V) [45, 46]. A large-scale hydroponics study using 46 different plants suggested that the uptake of MMA and DMA was significantly less than As(V) absorption [47]. Among the NIP family, NIP2;1 was found to be permeable to the methylated As species in rice root [48]. Aquaporin OsLsi1 is known to carry out the influx of methylated As in roots of rice [45]. A severe decrease in the MMA and DMA uptake was observed in mutants of rice plants lacking the Lsi1 proteins. Additionally, expression of *OsLsi1* in *Xenopus. laevis* oocytes showed significant increase in MMA uptake as compared to control [45]. Moreover, methylated As species have also been shown to take up the entry route as glycerol in rice roots, suggesting an active role of aquaglyceroporins in MMA and DMA uptake [49].

**3.Effect of Arsenic on Plants:**

*i) Growth and development.* Accumulation of As significantly affect the plant productivity by inhibiting overall plant growth and development thereby effecting the productivity (Figure 1). As toxicity inhibit seed germination and early seedling growth [21, 50]. Stunted growth with fewer side branches and decrease in fresh weight has been reported with increase in accumulation of As in plants [51, 52]. As toxicity during early seedling development also results in stunted root and shoot growth [53, 54]. Exposure of As also alter leaf development, such as reduction in leaf area and size [52, 55]. The As accumulation also reduces the number of tillers and seed weight in rice thereby retarding its yield [56].

*ii) Photosynthesis.* Increase in As accumulation severely affect the productivity in plant by causing perturbation in structural and functional units of photosynthetic process. A decrease in chlorophyll concentration due to hinderance in the chlorophyll biosynthesis was observed under As stress [57-59]. A decrease in the level of chlorophyll biosynthesis precursors, such as, protoporphyrin IX, Mg-protoporphyrin, Mg-protoporphyrin methyl ester, and divinyl protochlorophyllide, was observed due increase in As accumulation. Reduction in photosynthetic pigment concentration slower the rate of efficient excitation transfer towards the reaction center II (RCII) thereby resulting in higher non-photochemical quenching (NPQ) by light harvesting complex II (LHCII). Increase in As in plants also effects the heat dissipation capacity in plants [60]. Accumulation of starch was also observed in response to As toxicity, suggesting a inhibition in downstream starch consumption processes [52]. As toxicity also causes perturbation of chloroplast membrane thereby indirectly effecting the photosynthetic processes [61]. A decrease in CO2 fixation and PSII activity was also reported due to As toxicity. A decrease in the protein content of larger subunit of RuBisCO (LSU) in rice leaves was observed due to As toxicity [62].

*iii). Pi associated cellular processes.* Since As and Pi are chemically analogues, As gain its entry through the Pi transporter and perturb critical phosphate-dependent cellular processes. This perturbation is primarily via the replacement of Pi by As in biochemical processes [63, 64]. Oxidative phosphorylation and photophosphorylation occurring via electron transport chain (ETC) in mitochondria and chloroplast, respectively, are important reactions requiring Pi for the phosphorylation of ADP to ATP catalyzed by ATP synthases. Under high abundance of available As(V), the mitochondrial ATP synthases incorporate As(V) instead of Pi to generate ADP-As(V). The highly unstable ADP-As(V) undergoes rapid hydrolysis thus setting up a futile reaction cycle during photophosphorylation and oxidative phosphorylation thereby decreasing the ATP production in cell [65]. Since Pi is important for various biochemical processes and a critical component of biomolecules such as DNA and RNA, an As accumulation in cell leads to impairment of DNA/RNA metabolism, phospholipid metabolism, phosphorylation processes [63].

*iv) Reactive oxygen species (ROS) homeostasis.*  The ROS, such as superoxide radicle (O2‾), singlet oxygen (1O2), hydrogen peroxide (H2O2) and hydroxyl radicals (OH), are very critical by-products of the cellular processes that are responsible for plant development and its response to biotic and abiotic stresses [66-68]. The membranes, mitochondria, chloroplast and peroxisomes, contribute to a significant amount of the ROS generated in the cell. In chloroplast, mitochondrial and peroxisomes, the ETC are prominent site of O2‾production [67, 69, 70] Additionally, a significant amount of O2‾is also produced in peroxisomes during oxidation of xanthin and hypoxanthine in its matrix [69]. Peroxisomes are also a major house of production for the H2O2. A homeostasis is maintained in ROS generation and scavenging and any imbalance in the ROS concentration due to oxidative stresses can cause severe impairment of various cellular pathways. Arsenic accumulation results in more ROS production by stimulating ROS-producing enzymes, inhibiting the activity of enzymes involved in ETC and inactivation of antioxidative enzymes in the cell [71]. An increase in ROS mounts to an elevated oxidative damage to lipid, proteins, nucleic acids and carbohydrates [66, 72, 73]. Membrane damage and leakage also increase due to oxidation of membrane lipids under As stress. This increase in ROS due to As is known to impair development of seed, embryo, seedling and root development in plants [60, 74]. Disruption of the cell division process due to elevated ROS has been identified as one of the primary effects of As toxicity in plants [75, 76]. Increase in ROS due to As accumulation also triggers a overwhelmed plant defense mechanism which leads to cell death [77].

*iv) Metabolism.* Increased As accumulation has been shown to affect the carbohydrate, protein, lipid metabolism thereby limiting plant growth and development. An accumulation of starch and sugar due to decrease in their metabolism was observed under As toxicity in rice [10]. Inhibition of the starch degrading enzymes, alpha- amylase, beta-amylase and starch phosphorylase, was reported under As stress. Hydrolysis of starch to maltose and glucose and phosphorylation of glucose by hexokinase is critical for the glycolysis process [78]. The As toxicity leads to inhibition of amylolytic activity thereby decreasing the generation of maltose from sucrose. As(V) interfere with the phosphorylation reaction involving breaking down of starch and maltose to generate glucose-1-As(V) which needs to be phosphorylated at the expense of ATP before entering glycolysis thus resulting in a net decrease in energetic yield in cells.

Lipid peroxidation is one of the major effects of the As stress in plant that leads to cellular and organelle membrane perturbation thereby resulting in increased leakage of electrolytes and other essential components [79]. The lipid peroxidation induced by As accumulation also generate malondialdehyde (MDA), 4-hydroxy-2-nonenal, hydroxyl and keto fatty acids which conjugates with proteins and DNA and impede their related function [80]. As accumulation also causes membrane disruption due to its affinity with sulfhydryl groups in membrane proteins thereby resulting in cell death [81]. The proteolytic activity of proteases and peptidases are also inhibited in seeds, seedlings and cotyledons in As-stressed conditions thereby effecting growth and development [82]. The ROS generated by As toxicity also oxidize amino acids which alters and/or inhibit protein activity which in turn also render proteins susceptible to proteolytic attack [83].

**4.Effect of Arsenic on human body organs:**

*i) Skin.* Exposure to arsenic for a long duration first affects the skin causing pigmentation changes, skin lesions along with hard patches on the palms and soles of feet. Arsenic accumulates in keratin rich tissues such as skin hair and nails due to its affinity for sulfhydryl groups in cysteine-rich proteins [1]. Arsenic level in hair and nail may be used as an indicator of post arsenic exposure. Sometimes single solid transverse white band on nails (Mee’s line) appears as an indication of arsenic exposure. Moreover, in human keratinocyte arsenic is responsible for loss of function in DNA ligase that is involved in DNA repair pathway thereby making these cells more prone to mutations [84]. Thus, long term exposure to arsenic is associated with skin lesions (pigmentation, depigmentation and keratosis) and skin carcinoma (Figure2) [2].

*ii) Lungs.* Inhalation of arsenic dust in mining and smelting industries is often associated with irritation of the mucus membrane. Chronic exposure to arsenic can result in bronchitis, rhinitis, tracheobronchial mucosal and sub-mucosal hemorrhages and chronic cough [2, 85, 86]. The chance of laryngeal (LC) and nasopharyngeal (NPC) cancer development is related to the level of arsenic in blood [87]. Chronic exposure to arsenic compound can cause lung cancer [88]. Arsenic causes polarization to inflammation causing M2 macrophages thereby resulting in lung tumorigenesis [89]

*iii) Kidney.* Kidney is the major organ through which arsenic excretion takes place. It is also a major site of conversion of pentavalent arsenic into the more toxic and less soluble trivalent arsenic. Accumulation of arsenic in the kidney is responsible for damage to renal capillaries as well as renal tubules due to enhanced ROS production and increase in the levels of proinflammatory cytokines such as tumor necrosis factor alpha as well as interleukin-6 [90]. It is also associated with nephrotoxicity and chronic kidney disease (CKD) resulting in reduced glomerular filtration rate. Moreover, albuminuria and proteinuria is also observed due to injury of the renal podocytes [91, 92]. Subsequently, long term exposure to arsenic can cause renal cell carcinoma by influencing the miR-182-5p/HIF2α pathway [93]. Accumulation of arsenic in urinary bladder epithelium is responsible for enhanced cell proliferation thereby resulting in bladder cancer [94, 95].

**Figure 2.** Schematic representation of effects of As toxicity on human body.

*iv)* *Liver.* After absorption of arsenic compounds from food through the gastrointestinal tract, it ﬁrst reaches the liver. In liver, arsenic is detoxified via glutathione, and excreted in bile. It can also be methylated by arsenicmethyltransferase and finally excreted in urine [96]. Liver accumulates arsenic with repeated exposures [96]. Thus, hepatic disease (abnormal liver function, hepatomegaly, hepatoportal sclerosis, liver ﬁbrosis and cirrhosis) is reported as the most common complication of chronic exposures to arsenic [97, 98]. Studies on mouse model of arsenic toxicity have identified liver to be in a state of chronic inflammation [92]. The association between environmental arsenic exposure and human liver cancer has also been repeatedly reported [99]. The mechanism of hepatocarcinogenesis include oxidative DNA damage, acquired tolerance to apoptosis, enhanced cell proliferation, altered DNA methylation and genomic instability [98].

*v) Brain and Nervous system.* Arsenic accumulation in brain has been reported to cause impairment of neurological functioning such as intelligence, learning, short term memory and concentration [100, 101]. Chronic arsenic exposure commonly causes peripheral neuropathy [18]. It involves numbness and parasthesia, diminished sensation of touch, pain, heat, cold and muscle weakness [102]. Arsenic causes reduction in antioxidant enzymes followed by generation of free radical in brain tissue resulting in an increase in lipid peroxidation levels causing neurotoxicity [103]. Since arsenic is capable of crossing the placenta, its concentration is same in cord and maternal blood among pregnant women living in arsenic contaminated area [104]. Once arsenic gains access to the neonate, it may directly affect the central nervous system by crossing the blood-brain-barrier (BBB) [105]. Arsenic causes astrocyte death leading to increased permeability of BBB to toxicants [106]. Prenatal and early postnatal exposure to arsenic have been shown to be associated with reduced brain weight, decreased number of glia and neurons, defects in neural tube and changes in neurotransmitter system resulting in significant spatial memory impairment [107].

*vi) Reproductive organ.* In males, inorganic arsenic cause reproductive dysfunction including reduction in the size of testis, accessory sex organ and sperm count which in turn is associated with male infertility [108]. Moreover, the concentrations of luteinizing hormone (LH), follicle stimulating hormone (FSH), and testosterone is found to reduce after exposure to arsenic thereby resulting in impaired spermatogenesis [108]. Studies have shown prostate cancer to be associated with arsenic ingestion [109]. In females, arsenic caused reduction in ovarian weight, mean uterine diameter, decrease in endometrium and myometrium thickness. This was accompanied by lower levels of plasma estradiol, progesterone, FSH and LH in rat model of arsenic toxicity [2, 110].

*vii) Immune system.* People in higher arsenic exposed area have higher risk of certain types of cancer but also higher incidence of opportunistic infections, parasitosis, development of allergies and asthma [86, 111-113]. Arsenic disrupts both the innate and adaptive arm of the immune system thereby resulting in carcinogenesis [114]. It inhibits the function of macrophage and causes change in expression of secreted cytokines such as TNFA, IFNG, IL2, IL10, IL5, and IL4 by activated T lymphocyte cells [115-117]. Arsenic also induced the activation of regulatory T cells which caused immunosuppression [113]. Choudhury et.al. showed high dose of arsenic causes modulation of NF-κB signaling which results in enhanced immune-suppression [118]. Arsenic exposure is also responsible for a state of chronic inflammation thereby increasing the susceptibility of a person to pathogenic infections and cancer development[119].

*viii) Blood and cardiovascular system.* Long term exposure to arsenic is found to be associated with increased mortality from cardiovascular disease [92]. Anemia and leukopenia is frequently associated with chronic arsenic exposure [120]. Anemia is due to the role of arsenic in disrupting the differentiation of erythrocytes by inhibiting the function of GATA-1 transcription factor [121]. Arsenic causes changes in the platelet cytoskeleton network which makes them more prone to activating stimuli thereby contributing to enhanced thrombosis [122]. Increased platelet aggregation and reduction in fibrinolysis results in increased risk of atherosclerosis on chronic exposure to arsenic [123]. Furthermore, arsenic exposed individuals show high prevalence of ischemic heart disease, cardiac arrhythmias and hypertrophy of the ventricular muscles [124, 125].

*ix) Mechanism of action.* Arsenic exposure increases the production of reactive oxygen species (ROS). Reactive oxygen and nitrogen species such as superoxide anion, peroxyl radical, hydrogen peroxide, hydroxyl radical, and nitric oxide are responsible for causing mutation in the genome of an organism which may lead to carcinogenesis [125]. Studies suggest that arsenic causes morphological changes in mitochondria which is the source of increased intracellular ROS [125]. It also causes impairment in the DNA repair pathway enzymes such as XPC thereby enhancing the observed genotoxic effect of arsenic [126, 127]. The activity of E2F1 transcription factor, that regulate cell cycle progression, is inhibited by arsenic via phosphorylation of retinoblastoma protein [128]. Arsenic can lead to DNA hypermethylation thereby lowering gene expression [129]. Arsenic can induce apoptosis by modulating LncRNA MEG3 expression [130].

**5.Conclusion and Future Perspective:**

In India, many states have ground water arsenic contamination due to which crop productivity is reduced and there is a serious hazardous effect on human health. The As accumulation not only impair growth and development in plants but also is a major cause of biomagnification in humans. Thus, the aim to reduce As accumulation in plants will serve the dual-purpose of sustaining the crop productivity and act as a solution to the As biomagnification concern in humans. One of the major biotechnological approach is modulation in the abundance of As associated transporters (including both influx and efflux transporters) and metabolic processes. Overexpression of the Pi transporter which has higher preference of Pi over As will help in uninterrupted supply of the Pi required for growth and development in plants without elevating the As concentration [131]. In a reverse approach, downregulation of Pi transporter which have higher affinity for As has also been shown to result in lesser As accumulation and enhanced As stress tolerance in crop plants [25]. Ectopic expression of the proteins responsible for As efflux from cells are also widely used technique to achieve As tolerance [132]. Manipulation of As metabolism to generate more of the volatile form of As is also a desirable approach to reduce As accumulation in crop plants [133-135]. Overexpression of AsIII S-adenosylmethionine methyltransferase (ArsM), an enzyme responsible for As biomethylation, in rice led to lesser accumulation of arsenic. Since the microorganism population of the soil and groundwater control the nutrient availability of the plants, bio-augmentation and bio-stimulation approaches are also widely implemented for reducing the As accumulation in the environment [136-138]. Use of large-scale genome analysis tools to identify a greater number of genes responsible for As tolerance and exploiting new gene editing tools such as CRISPR-Cas9 may prove beneficiary in the crop biotechnology field in reducing the As accumulation problem. In humans, dietary nutrients such as proteins, iron, zinc and vitamins result in increased urinary excretion of arsenic thereby reducing the toxic effects of the heavy metal. Thus, individuals residing in the arsenic endemic areas should maintain a healthy nutritional status in order to reduce the toxic effects associated with arsenic-contaminated food and water. Simultaneous multifaceted approaches, including public awareness to reduce As contamination by human and ecological means to decontaminate the environment is also required to reduce As toxicity.

**References:**

[1] Shen S, Li XF, Cullen WR, Weinfeld M, Le XC. Arsenic binding to proteins. Chem Rev 2013;113:7769-92.

[2] Kapaj S, Peterson H, Liber K, Bhattacharya P. Human health effects from chronic arsenic poisoning--a review. J Environ Sci Health A Tox Hazard Subst Environ Eng 2006;41:2399-428.

[3] Tchounwou PB, Yedjou CG, Udensi UK, Pacurari M, Stevens JJ, Patlolla AK, Noubissi F, Kumar S. State of the science review of the health effects of inorganic arsenic: Perspectives for future research. Environ Toxicol 2019;34:188-202.

[4] Abdul KS, Jayasinghe SS, Chandana EP, Jayasumana C, De Silva PM. Arsenic and human health effects: A review. Environ Toxicol Pharmacol 2015;40:828-46.

[5] Mann RV, Martina & Peijnenburg, Willie. . Metals and Metalloids in Terrestrial Systems: Bioaccumulation,Biomagnification and Subsequent Adverse Effects, 2011.

[6] Zhao FJ, McGrath SP, Meharg AA. Arsenic as a food chain contaminant: mechanisms of plant uptake and metabolism and mitigation strategies. Annu Rev Plant Biol 2010;61:535-59.

[7] Shankar S, Shanker U, Shikha. Arsenic contamination of groundwater: a review of sources, prevalence, health risks, and strategies for mitigation. ScientificWorldJournal 2014;2014:304524.

[8] Matschullat J. Arsenic in the geosphere--a review. Sci Total Environ 2000;249:297-312.

[9] Punshon T, Jackson BP, Meharg AA, Warczack T, Scheckel K, Guerinot ML. Understanding arsenic dynamics in agronomic systems to predict and prevent uptake by crop plants. Sci Total Environ 2017;581-582:209-20.

[10] Jha AB, Dubey RS. Carbohydrate metabolism in growing rice seedlings under arsenic toxicity. J Plant Physiol 2004;161:867-72.

[11] Gautam A, Pandey AK, Dubey RS. Azadirachta indica and Ocimum sanctum leaf extracts alleviate arsenic toxicity by reducing arsenic uptake and improving antioxidant system in rice seedlings. Physiol Mol Biol Plants 2020;26:63-81.

[12] Shri M, Singh PK, Kidwai M, Gautam N, Dubey S, Verma G, Chakrabarty D. Recent advances in arsenic metabolism in plants: current status, challenges and highlighted biotechnological intervention to reduce grain arsenic in rice. Metallomics 2019;11:519-32.

[13] Jha A, and Dubey, R. . Effect of arsenic on behaviour of enzymes of sugar metabolism in germinating rice seeds. Acta Physiologiae Plantarum 2005;27:341-47.

[14] Kashyap L, & Garg, N. . Arsenic Toxicity in Crop Plants: Responses and Remediation Strategies. Mechanisms of Arsenic Toxicity and Tolerance in Plants 2018:129-69.

[15] Gautam AP, Akhilesh & Dubey, Rama. . Effect of Arsenic Toxicity on Photosynthesis, Oxidative Stress and Alleviation of Toxicitywith Herbal Extracts in Growing Rice Seedlings. Indian Journal of Agricultural Biochemistry 2019;32.

[16] Vieira C, Morais S, Ramos S, Delerue-Matos C, Oliveira MB. Mercury, cadmium, lead and arsenic levels in three pelagic fish species from the Atlantic Ocean: intra- and inter-specific variability and human health risks for consumption. Food Chem Toxicol 2011;49:923-32.

[17] Leonard A, Lauwerys RR. Carcinogenicity, teratogenicity and mutagenicity of arsenic. Mutat Res 1980;75:49-62.

[18] Ratnaike RN. Acute and chronic arsenic toxicity. Postgrad Med J 2003;79:391-6.

[19] Weber FA, Hofacker AF, Voegelin A, Kretzschmar R. Temperature dependence and coupling of iron and arsenic reduction and release during flooding of a contaminated soil. Environ Sci Technol 2010;44:116-22.

[20] Neumann RB, Seyfferth AL, Teshera-Levye J, Ellingson J. Soil Warming Increases Arsenic Availability in the Rice Rhizosphere. Agricultural & Environmental Letters 2017;2:170006.

[21] Abedin MJ, Feldmann J, Meharg AA. Uptake kinetics of arsenic species in rice plants. Plant Physiol 2002;128:1120-8.

[22] Ma JF, Yamaji N, Mitani N, Xu XY, Su YH, McGrath SP, Zhao FJ. Transporters of arsenite in rice and their role in arsenic accumulation in rice grain. Proc Natl Acad Sci U S A 2008;105:9931-5.

[23] Zhao XQ, Mitani N, Yamaji N, Shen RF, Ma JF. Involvement of silicon influx transporter OsNIP2;1 in selenite uptake in rice. Plant Physiol 2010;153:1871-7.

[24] Xu W, Dai W, Yan H, Li S, Shen H, Chen Y, Xu H, Sun Y, He Z, Ma M. Arabidopsis NIP3;1 Plays an Important Role in Arsenic Uptake and Root-to-Shoot Translocation under Arsenite Stress Conditions. Mol Plant 2015;8:722-33.

[25] Cao Y, Sun D, Ai H, Mei H, Liu X, Sun S, Xu G, Liu Y, Chen Y, Ma LQ. Knocking Out OsPT4 Gene Decreases Arsenate Uptake by Rice Plants and Inorganic Arsenic Accumulation in Rice Grains. Environ Sci Technol 2017;51:12131-8.

[26] Chen Y, Han YH, Cao Y, Zhu YG, Rathinasabapathi B, Ma LQ. Arsenic Transport in Rice and Biological Solutions to Reduce Arsenic Risk from Rice. Front Plant Sci 2017;8:268.

[27] Mukhopadhyay R, Bhattacharjee H, Rosen BP. Aquaglyceroporins: generalized metalloid channels. Biochim Biophys Acta 2014;1840:1583-91.

[28] Li G, Santoni V, Maurel C. Plant aquaporins: roles in plant physiology. Biochim Biophys Acta 2014;1840:1574-82.

[29] Zhao FJ, Ma JF, Meharg AA, McGrath SP. Arsenic uptake and metabolism in plants. New Phytol 2009;181:777-94.

[30] Bienert GP, Thorsen M, Schussler MD, Nilsson HR, Wagner A, Tamas MJ, Jahn TP. A subgroup of plant aquaporins facilitate the bi-directional diffusion of As(OH)3 and Sb(OH)3 across membranes. BMC Biol 2008;6:26.

[31] Kamiya T, Fujiwara T. Arabidopsis NIP1;1 transports antimonite and determines antimonite sensitivity. Plant Cell Physiol 2009;50:1977-81.

[32] Katsuhara M, Sasano S, Horie T, Matsumoto T, Rhee J, Shibasaka M. Functional and molecular characteristics of rice and barley nip aquaporins transporting water, hydrogen peroxide and arsenite. Plant Biotechnology 2014;31:312-19.

[33] Mosa KA, Kumar K, Chhikara S, McDermott J, Liu Z, Musante C, White JC, Dhankher OP. Members of rice plasma membrane intrinsic proteins subfamily are involved in arsenite permeability and tolerance in plants. Transgenic Res 2012;21:1265-77.

[34] Asher CJ, PF R. Arsenic uptake by barley seedlings. Australian Journal of Plant Physiology 1979;6:459-66.

[35] Shin H, Shin HS, Dewbre GR, Harrison MJ. Phosphate transport in Arabidopsis: Pht1;1 and Pht1;4 play a major role in phosphate acquisition from both low- and high-phosphate environments. Plant J 2004;39:629-42.

[36] Catarecha P, Segura MD, Franco-Zorrilla JM, Garcia-Ponce B, Lanza M, Solano R, Paz-Ares J, Leyva A. A mutant of the Arabidopsis phosphate transporter PHT1;1 displays enhanced arsenic accumulation. Plant Cell 2007;19:1123-33.

[37] Fontenot EB, Ditusa SF, Kato N, Olivier DM, Dale R, Lin WY, Chiou TJ, Macnaughtan MA, Smith AP. Increased phosphate transport of Arabidopsis thaliana Pht1;1 by site-directed mutagenesis of tyrosine 312 may be attributed to the disruption of homomeric interactions. Plant Cell Environ 2015;38:2012-22.

[38] Jia H, Ren H, Gu M, Zhao J, Sun S, Zhang X, Chen J, Wu P, Xu G. The phosphate transporter gene OsPht1;8 is involved in phosphate homeostasis in rice. Plant Physiol 2011;156:1164-75.

[39] Wu Z, Ren H, McGrath SP, Wu P, Zhao FJ. Investigating the contribution of the phosphate transport pathway to arsenic accumulation in rice. Plant Physiol 2011;157:498-508.

[40] Ma LQ, Komar KM, Tu C, Zhang W, Cai Y, Kennelley ED. A fern that hyperaccumulates arsenic. Nature 2001;409:579.

[41] DiTusa SF, Fontenot EB, Wallace RW, Silvers MA, Steele TN, Elnagar AH, Dearman KM, Smith AP. A member of the Phosphate transporter 1 (Pht1) family from the arsenic-hyperaccumulating fern Pteris vittata is a high-affinity arsenate transporter. New Phytol 2016;209:762-72.

[42] Thomas DJ, Waters SB, Styblo M. Elucidating the pathway for arsenic methylation. Toxicol Appl Pharmacol 2004;198:319-26.

[43] Huang H, Jia Y, Sun GX, Zhu YG. Arsenic speciation and volatilization from flooded paddy soils amended with different organic matters. Environ Sci Technol 2012;46:2163-8.

[44] Huang JH. Impact of Microorganisms on Arsenic Biogeochemistry:A Review. Water Air Soil Pollution 2014;225:1845.

[45] Li RY, Ago Y, Liu WJ, Mitani N, Feldmann J, McGrath SP, Ma JF, Zhao FJ. The rice aquaporin Lsi1 mediates uptake of methylated arsenic species. Plant Physiol 2009;150:2071-80.

[46] Jia Y, Huang H, Sun GX, Zhao FJ, Zhu YG. Pathways and relative contributions to arsenic volatilization from rice plants and paddy soil. Environ Sci Technol 2012;46:8090-6.

[47] Raab A, Williams PN, Meharg A, Feldmann J. Uptake and translocation of inorganic and methylated arsenic species by plants. Environmental Chemistry 2007;4:197-203.

[48] Ma JF, Yamaji N. Silicon uptake and accumulation in higher plants. Trends Plant Sci 2006;11:392-7.

[49] Rahman MA, Kadohashi K, Maki T, Hasegawa H. Transport of DMAA and MMAA into rice (Oryza sativa L.) roots. Environmental and Experimental Botany 2011;72:41-6.

[50] Mahdieh S, Ghaderian SM, Karimi N. Effect of arsenic on germination, photosynthesis and growth parameters of two winter wheat varieties in Iran. Journal of Plant Nutrition 2013;36:651-64.

[51] Monteiro C, Santos C, Pinho S, Oliveira H, Pedrosa T, Dias MC. Cadmium-induced cyto- and genotoxicity are organ-dependent in lettuce. Chem Res Toxicol 2012;25:1423-34.

[52] Mishra S, Stark HJ, Kupper H. A different sequence of events than previously reported leads to arsenic-induced damage in Ceratophyllum demersum L. Metallomics 2014;6:444-54.

[53] Malik JA, Goel S, Sandhir R, Nayyar H. Uptake and Distribution of Arsenic in Chickpea: Effects on Seed Yield and Seed Composition. Communications in Soil Science and Plant Analysis 2011;42:1728-38.

[54] Vromman D, Lutts S, Lefèvre I, Somer L, De Vreese O, Šlejkovec Z, Quinet M. Effects of simultaneous arsenic and iron toxicities on rice (Oryza sativa L.) development, yield-related parameters and As and Fe accumulation in relation to As speciation in the grains. Plant and Soil 2013;371:199-217.

[55] Nath S, Panda P, Mishra S, Dey M, Choudhury S, Sahoo L, Panda SK. Arsenic stress in rice: redox consequences and regulation by iron. Plant Physiol Biochem 2014;80:203-10.

[56] Bag MK, Adhikari B, Dwivedi S, Tripathi RD. Consequences of arsenate exposure on important yield-associated traits of rice (Oryza sativa L.). Journal of Plant Science & Research 2014;1:109.

[57] Kumari A, Pandey N, Pandey-Rai S. Exogenous salicylic acid-mediated modulation of arsenic stress tolerance with enhanced accumulation of secondary metabolites and improved size of glandular trichomes in Artemisia annua L. Protoplasma 2018;255:139-52.

[58] Emamverdian A, Ding Y, Mokhberdoran F, Xie Y. Heavy metal stress and some mechanisms of plant defense response. The Scientific World Journal 2015;2015.

[59] Mishra S, Dwivedi S, Kumar A, Chauhan R, Awasthi S, Mattusch J, RD T. Current status of ground water arsenic contamination in India and recent advancements in removal techniques from drinking water. INTERNATIONAL JOURNAL OF PLANT AND ENVIRONMENT 2016;2.

[60] Chandrakar V, Dubey A, Keshavkant S. Modulation of antioxidant enzymes by salicylic acid in arsenic exposed Glycine max L. J. Journal of Soil Science and Plant Nutrition 2016;16:662-76.

[61] Rafiq M, Shahid M, Abbas G, Shamshad S, Khalid S, Niazi NK, Dumat C. Comparative effect of calcium and EDTA on arsenic uptake and physiological attributes of Pisum sativum. Int J Phytoremediation 2017;19:662-9.

[62] Ahsan N, Lee DG, Kim KH, Alam I, Lee SH, Lee KW, Lee H, Lee BH. Analysis of arsenic stress-induced differentially expressed proteins in rice leaves by two-dimensional gel electrophoresis coupled with mass spectrometry. Chemosphere 2010;78:224-31.

[63] Finnegan PM, Chen W. Arsenic toxicity: the effects on plant metabolism. Front Physiol 2012;3:182.

[64] Abbas G, Murtaza B, Bibi I, Shahid M, Niazi NK, Khan MI, Amjad M, Hussain M, Natasha. Arsenic Uptake, Toxicity, Detoxification, and Speciation in Plants: Physiological, Biochemical, and Molecular Aspects. Int J Environ Res Public Health 2018;15.

[65] Tawfik DS, Viola RE. Arsenate replacing phosphate: alternative life chemistries and ion promiscuity. Biochemistry 2011;50:1128-34.

[66] Huang H, Ullah F, Zhou DX, Yi M, Zhao Y. Mechanisms of ROS Regulation of Plant Development and Stress Responses. Front Plant Sci 2019;10:800.

[67] Karuppanapandian T, Moon J-C, Kim C, Manoharan K, Kim W. Reactive oxygen species in plants: Their generation, signal transduction, and scavenging mechanisms. Australian Journal of Crop Science 2011;5:709-25.

[68] Das K, Roychoudhury A. Reactive oxygen species (ROS) and response of antioxidants as ROS-scavengers during environmental stress in plants. Frontiers in Environmental Science 2014;2.

[69] Del Rio LA, Lopez-Huertas E. ROS Generation in Peroxisomes and its Role in Cell Signaling. Plant Cell Physiol 2016;57:1364-76.

[70] Rhoads DM, Umbach AL, Subbaiah CC, Siedow JN. Mitochondrial reactive oxygen species. Contribution to oxidative stress and interorganellar signaling. Plant Physiol 2006;141:357-66.

[71] Requejo R, Tena M. Proteome analysis of maize roots reveals that oxidative stress is a main contributing factor to plant arsenic toxicity. Phytochemistry 2005;66:1519-28.

[72] Flora SJ. Arsenic-induced oxidative stress and its reversibility. Free Radic Biol Med 2011;51:257-81.

[73] Shahid M, Pourrut B, Dumat C, Nadeem M, Aslam M, Pinelli E. Heavy-metal-induced reactive oxygen species: phytotoxicity and physicochemical changes in plants. Rev Environ Contam Toxicol 2014;232:1-44.

[74] da-Silva CJ, Canatto RA, Cardoso AA, Ribeiro C, JA O. Arsenic-hyperaccumulation and antioxidant system in the aquatic macrophyte Spirodela intermedia W. Koch (Lemnaceae). Theoretical and Experimental Plant Physiology 2017;29:203-13.

[75] Livanos P, Apostolakos P, Galatis B. Plant cell division: ROS homeostasis is required. Plant Signal Behav 2012;7:771-8.

[76] Livanos P, Galatis B, Quader H, Apostolakos P. Disturbance of reactive oxygen species homeostasis induces atypical tubulin polymer formation and affects mitosis in root-tip cells of Triticum turgidum and Arabidopsis thaliana. Cytoskeleton (Hoboken) 2012;69:1-21.

[77] Van Breusegem F, Dat JF. Reactive oxygen species in plant cell death. Plant Physiol 2006;141:384-90.

[78] Zeeman SC, Smith SM, Smith AM. The breakdown of starch in leaves. New Phytol 2004;163:247-61.

[79] Gill SS, Tuteja N. Reactive oxygen species and antioxidant machinery in abiotic stress tolerance in crop plants. Plant Physiol Biochem 2010;48:909-30.

[80] Parkhey S, Naithani SC, Keshavkant S. ROS production and lipid catabolism in desiccating Shorea robusta seeds during aging. Plant Physiol Biochem 2012;57:261-7.

[81] Meharg AA, Hartley-Whitaker, J. Arsenic uptake and metabolism in arsenic resistant and nonresistant plant species. New Phytologist 2002;154:29-43.

[82] Mascher RL, B.; Holzinger, S.; Bergmann, H. Arsenate toxicity: effects on oxidative stress response molecules and enzymes in red clover plants. Plant Science 2002;163:961-69.

[83] Moller IM, Jensen PE, Hansson A. Oxidative modifications to cellular components in plants. Annu Rev Plant Biol 2007;58:459-81.

[84] Li JH, Rossman TG. Inhibition of DNA ligase activity by arsenite: a possible mechanism of its comutagenesis. Mol Toxicol 1989;2:1-9.

[85] Milton AH, Rahman M. Respiratory effects and arsenic contaminated well water in Bangladesh. Int J Environ Health Res 2002;12:175-9.

[86] Tsai TL, Lei WT, Kuo CC, Sun HL, Su PH, Wang SL. Maternal and childhood exposure to inorganic arsenic and airway allergy - A 15-Year birth cohort follow-up study. Environ Int 2021;146:106243.

[87] Khlifi R, Olmedo P, Gil F, Molka FT, Hammami B, Ahmed R, Amel HC. Risk of laryngeal and nasopharyngeal cancer associated with arsenic and cadmium in the Tunisian population. Environ Sci Pollut Res Int 2014;21:2032-42.

[88] Hong YS, Song KH, Chung JY. Health effects of chronic arsenic exposure. J Prev Med Public Health 2014;47:245-52.

[89] Cui J, Xu W, Chen J, Li H, Dai L, Frank JA, Peng S, Wang S, Chen G. M2 polarization of macrophages facilitates arsenic-induced cell transformation of lung epithelial cells. Oncotarget 2017;8:21398-409.

[90] Wang Y, Zhao H, Shao Y, Liu J, Li J, Xing M. Copper or/and arsenic induce oxidative stress-cascaded, nuclear factor kappa B-dependent inflammation and immune imbalance, trigging heat shock response in the kidney of chicken. Oncotarget 2017;8:98103-16.

[91] Robles-Osorio ML, Sabath-Silva E, Sabath E. Arsenic-mediated nephrotoxicity. Ren Fail 2015;37:542-7.

[92] States JC, Srivastava S, Chen Y, Barchowsky A. Arsenic and cardiovascular disease. Toxicol Sci 2009;107:312-23.

[93] Fang X, Sun R, Hu Y, Wang H, Guo Y, Yang B, Pi J, Xu Y. miRNA-182-5p, via HIF2alpha, contributes to arsenic carcinogenesis: evidence from human renal epithelial cells. Metallomics 2018;10:1607-17.

[94] Mendez WM, Jr., Eftim S, Cohen J, Warren I, Cowden J, Lee JS, Sams R. Relationships between arsenic concentrations in drinking water and lung and bladder cancer incidence in U.S. counties. J Expo Sci Environ Epidemiol 2017;27:235-43.

[95] Luster MI, Simeonova PP. Arsenic and urinary bladder cell proliferation. Toxicol Appl Pharmacol 2004;198:419-23.

[96] Khairul I, Wang QQ, Jiang YH, Wang C, Naranmandura H. Metabolism, toxicity and anticancer activities of arsenic compounds. Oncotarget 2017;8:23905-26.

[97] Santra A, Maiti A, Das S, Lahiri S, Charkaborty SK, Mazumder DN. Hepatic damage caused by chronic arsenic toxicity in experimental animals. J Toxicol Clin Toxicol 2000;38:395-405.

[98] Liu J, Waalkes MP. Liver is a target of arsenic carcinogenesis. Toxicol Sci 2008;105:24-32.

[99] Wang W, Cheng S, Zhang D. Association of inorganic arsenic exposure with liver cancer mortality: A meta-analysis. Environ Res 2014;135:120-5.

[100] Tyler CR, Allan AM. The Effects of Arsenic Exposure on Neurological and Cognitive Dysfunction in Human and Rodent Studies: A Review. Curr Environ Health Rep 2014;1:132-47.

[101] Pandey R, Rai V, Mishra J, Mandrah K, Kumar Roy S, Bandyopadhyay S. From the Cover: Arsenic Induces Hippocampal Neuronal Apoptosis and Cognitive Impairments via an Up-Regulated BMP2/Smad-Dependent Reduced BDNF/TrkB Signaling in Rats. Toxicol Sci 2017;159:137-58.

[102] Mochizuki H, Phyu KP, Aung MN, Zin PW, Yano Y, Myint MZ, Thit WM, Yamamoto Y, Hishikawa Y, Thant KZ, Maruyama M, Kuroda Y. Peripheral neuropathy induced by drinking water contaminated with low-dose arsenic in Myanmar. Environ Health Prev Med 2019;24:23.

[103] Flora SJ, Bhadauria S, Pant SC, Dhaked RK. Arsenic induced blood and brain oxidative stress and its response to some thiol chelators in rats. Life Sci 2005;77:2324-37.

[104] Navasumrit P, Chaisatra K, Promvijit J, Parnlob V, Waraprasit S, Chompoobut C, Binh TT, Hai DN, Bao ND, Hai NK, Kim KW, Samson LD, Graziano JH, Mahidol C, Ruchirawat M. Exposure to arsenic in utero is associated with various types of DNA damage and micronuclei in newborns: a birth cohort study. Environ Health 2019;18:51.

[105] Tolins M, Ruchirawat M, Landrigan P. The developmental neurotoxicity of arsenic: cognitive and behavioral consequences of early life exposure. Ann Glob Health 2014;80:303-14.

[106] Htike NT, Maekawa F, Soutome H, Sano K, Maejima S, Aung KH, Tokuda M, Tsukahara S. Arsenic Exposure Induces Unscheduled Mitotic S Phase Entry Coupled with Cell Death in Mouse Cortical Astrocytes. Front Neurosci 2016;10:297.

[107] Ramos-Chavez LA, Rendon-Lopez CR, Zepeda A, Silva-Adaya D, Del Razo LM, Gonsebatt ME. Neurological effects of inorganic arsenic exposure: altered cysteine/glutamate transport, NMDA expression and spatial memory impairment. Front Cell Neurosci 2015;9:21.

[108] Kim YJ, Kim JM. Arsenic Toxicity in Male Reproduction and Development. Dev Reprod 2015;19:167-80.

[109] Roh T, Lynch CF, Weyer P, Wang K, Kelly KM, Ludewig G. Low-level arsenic exposure from drinking water is associated with prostate cancer in Iowa. Environ Res 2017;159:338-43.

[110] Akram Z, Jalali S, Shami SA, Ahmad L, Batool S, Kalsoom O. Adverse effects of arsenic exposure on uterine function and structure in female rat. Exp Toxicol Pathol 2010;62:451-9.

[111] Martinez VD, Vucic EA, Becker-Santos DD, Gil L, Lam WL. Arsenic exposure and the induction of human cancers. J Toxicol 2011;2011:431287.

[112] Farzan SF, Korrick S, Li Z, Enelow R, Gandolfi AJ, Madan J, Nadeau K, Karagas MR. In utero arsenic exposure and infant infection in a United States cohort: a prospective study. Environ Res 2013;126:24-30.

[113] Gera R, Singh V, Mitra S, Sharma AK, Singh A, Dasgupta A, Singh D, Kumar M, Jagdale P, Patnaik S, Ghosh D. Arsenic exposure impels CD4 commitment in thymus and suppress T cell cytokine secretion by increasing regulatory T cells. Sci Rep 2017;7:7140.

[114] Huang HW, Lee CH, Yu HS. Arsenic-Induced Carcinogenesis and Immune Dysregulation. Int J Environ Res Public Health 2019;16.

[115] Biswas R, Ghosh P, Banerjee N, Das JK, Sau T, Banerjee A, Roy S, Ganguly S, Chatterjee M, Mukherjee A, Giri AK. Analysis of T-cell proliferation and cytokine secretion in the individuals exposed to arsenic. Hum Exp Toxicol 2008;27:381-6.

[116] Banerjee N, Banerjee M, Ganguly S, Bandyopadhyay S, Das JK, Bandyopadhay A, Chatterjee M, Giri AK. Arsenic-induced mitochondrial instability leading to programmed cell death in the exposed individuals. Toxicology 2008;246:101-11.

[117] Lemarie A, Morzadec C, Bourdonnay E, Fardel O, Vernhet L. Human macrophages constitute targets for immunotoxic inorganic arsenic. J Immunol 2006;177:3019-27.

[118] Choudhury S, Gupta P, Ghosh S, Mukherjee S, Chakraborty P, Chatterji U, Chattopadhyay S. Arsenic-induced dose-dependent modulation of the NF-kappaB/IL-6 axis in thymocytes triggers differential immune responses. Toxicology 2016;357-358:85-96.

[119] Prasad P, Sinha D. Low-level arsenic causes chronic inflammation and suppresses expression of phagocytic receptors. Environ Sci Pollut Res Int 2017;24:11708-21.

[120] Islam LN, Nabi AH, Rahman MM, Khan MA, Kazi AI. Association of clinical complications with nutritional status and the prevalence of leukopenia among arsenic patients in Bangladesh. Int J Environ Res Public Health 2004;1:74-82.

[121] Zhou X, Medina S, Bolt AM, Zhang H, Wan G, Xu H, Lauer FT, Wang SC, Burchiel SW, Liu KJ. Inhibition of red blood cell development by arsenic-induced disruption of GATA-1. Sci Rep 2020;10:19055.

[122] Kim K, Shin EK, Chung JH, Lim KM. Arsenic induces platelet shape change through altering focal adhesion kinase-mediated actin dynamics, contributing to increased platelet reactivity. Toxicol Appl Pharmacol 2020;391:114912.

[123] Wang CH, Jeng JS, Yip PK, Chen CL, Hsu LI, Hsueh YM, Chiou HY, Wu MM, Chen CJ. Biological gradient between long-term arsenic exposure and carotid atherosclerosis. Circulation 2002;105:1804-9.

[124] Tseng CH, Chong CK, Tseng CP, Hsueh YM, Chiou HY, Tseng CC, Chen CJ. Long-term arsenic exposure and ischemic heart disease in arseniasis-hyperendemic villages in Taiwan. Toxicol Lett 2003;137:15-21.

[125] Jomova K, Jenisova Z, Feszterova M, Baros S, Liska J, Hudecova D, Rhodes CJ, Valko M. Arsenic: toxicity, oxidative stress and human disease. J Appl Toxicol 2011;31:95-107.

[126] Tam LM, Price NE, Wang Y. Molecular Mechanisms of Arsenic-Induced Disruption of DNA Repair. Chem Res Toxicol 2020;33:709-26.

[127] Holcomb N, Goswami M, Han SG, Scott T, D'Orazio J, Orren DK, Gairola CG, Mellon I. Inorganic arsenic inhibits the nucleotide excision repair pathway and reduces the expression of XPC. DNA Repair (Amst) 2017;52:70-80.

[128] Sheldon LA. Inhibition of E2F1 activity and cell cycle progression by arsenic via retinoblastoma protein. Cell Cycle 2017;16:2058-72.

[129] Ameer SS, Engstrom K, Hossain MB, Concha G, Vahter M, Broberg K. Arsenic exposure from drinking water is associated with decreased gene expression and increased DNA methylation in peripheral blood. Toxicol Appl Pharmacol 2017;321:57-66.

[130] Wang M, Tan J, Jiang C, Li S, Wu X, Ni G, He Y. Inorganic arsenic influences cell apoptosis by regulating the expression of MEG3 gene. Environ Geochem Health 2021;43:475-84.

[131] Cao Y, Sun D, Chen JX, Mei H, Ai H, Xu G, Chen Y, Ma LQ. Phosphate Transporter PvPht1;2 Enhances Phosphorus Accumulation and Plant Growth without Impacting Arsenic Uptake in Plants. Environ Sci Technol 2018;52:3975-81.

[132] Duan G, Kamiya T, Ishikawa S, Arao T, Fujiwara T. Expressing ScACR3 in rice enhanced arsenite efflux and reduced arsenic accumulation in rice grains. Plant Cell Physiol 2012;53:154-63.

[133] Meng XY, Qin J, Wang LH, Duan GL, Sun GX, Wu HL, Chu CC, Ling HQ, Rosen BP, Zhu YG. Arsenic biotransformation and volatilization in transgenic rice. New Phytol 2011;191:49-56.

[134] Verma S, Verma PK, Meher AK, Dwivedi S, Bansiwal AK, Pande V, Srivastava PK, Verma PC, Tripathi RD, Chakrabarty D. A novel arsenic methyltransferase gene of Westerdykella aurantiaca isolated from arsenic contaminated soil: phylogenetic, physiological, and biochemical studies and its role in arsenic bioremediation. Metallomics 2016;8:344-53.

[135] Deng F, Yamaji N, Ma JF, Lee SK, Jeon JS, Martinoia E, Lee Y, Song WY. Engineering rice with lower grain arsenic. Plant Biotechnol J 2018;16:1691-9.

[136] Chen J, Qin J, Zhu YG, de Lorenzo V, Rosen BP. Engineering the soil bacterium Pseudomonas putida for arsenic methylation. Appl Environ Microbiol 2013;79:4493-5.

[137] Chen J, Sun GX, Wang XX, Lorenzo V, Rosen BP, Zhu YG. Volatilization of arsenic from polluted soil by Pseudomonas putida engineered for expression of the arsM Arsenic(III) S-adenosine methyltransferase gene. Environ Sci Technol 2014;48:10337-44.

[138] Koonsom T, D I, S S, P T. Effect of kaolin on arsenic accumulation in rice plants (Oryza sativa L.) grown in arsenic contaminated soils. Environmental Engineering Research 2014;19:241-5.