Ecotoxicology and Environmental Safety xxx (xxxx) xxx-xxx

Contents lists available at ScienceDirect

Ecotoxicology and Environmental Safety

journal homepage: http://ees.elsevier.com

Review

Mechanisms of arsenic assimilation by plants and countermeasures to attenuate its accumulation in crops other than rice

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ARTICLE INFO

Keywords
Arsenic
Plant uptake
Food contamination
Mitigation strategies
Bioavailability
Bioaccessibility

ABSTRACT

Arsenic is a ubiquitous metalloid in the biosphere, and its origin can be either geogenic or anthropic. Four oxidation states (−3, 0, +3 and + 5) characterize organic and inorganic As- compounds. Although arsenic is reportedly a toxicant, its harmful effects are closely related to its chemical form: inorganic compounds are most toxic, followed by organic ones and finally by arsine gas. Although drinking water is the primary source of arsenic exposure to humans, the metalloid enters the food chain through its uptake by crops, the extent of which is tightly dependent on its phytoavailability. Arsenate is taken up by roots *via* phosphate carriers, while arsenite is taken up by a subclass of aquaporins (NIP), some of which involved in silicon (Si) transport. NIP and Si transporters are also involved in the uptake of methylated forms of As. Once taken up, its distribution is regulated by the same type of transporters albeit with mobility efficiencies depending on As forms and its accumulation generally occurs in the following decreasing order: roots > stems > leaves > fruits (seeds). Besides providing a survey on the uptake and transport mechanisms in higher plants, this review reports on measures able to reducing plant uptake and the ensuing transfer into edible parts. On the one hand, these measures include a variety of plant-based approaches including breeding, genetic engineering of transport systems, graft/rootstock combinations, and mycorrhization. On the other hand, they include agronomic practices with a particular focus on the use of inorganic and organic amendments, treatment of irrigation water, and fertilization.

1. Introduction

Due to its toxicity and carcinogenic properties to humans, arsenic is a contaminant of public concern. The oral intake of food and beverages is a widely relevant pathway of exposure to As while that of water is deemed to be the primary source in those regions where its content in drinking water exceeds 50 $\mu g\,L^{-1}$ (WHO/FAO, 2011). Apart from the threat due to the presence of arsenic in drinking water, the use of groundwater with high levels of this metalloid for irrigation purposes and the weathering of the parent material in diverse geographical areas have led to the accumulation of As in soils and, ultimately, to increased transfer of the metalloid into the food chains (Singh et al., 2015; Islam et al., 2017). For instance, in cereal crops, legumes and vegetables, the concentration ranges of accumulated As has been reported to amount to 0.07–0.83, 0.02–0.56 and 0.001–0.039 $mg\,kg^{-1}$, respectively (Pineda-Chacón and Alarcón-Herrera, 2016). Some estimates have suggested that the daily amount of arsenic consumed per capita may reach values as high as 0.9 mg (Butcher, 2009) and, according to the WHO, this value of daily intake is very close to the maximum tolerable limit (Williams et al., 2005). In addition to the hazard posed by the access of the metalloid into the food chain, plants that have undergone exposure to high concentrations, often manifest poisoning symptoms mainly due to the As-induced generation of reactive oxygen species and to the ability of As(III) to deactivate functional proteins (Abbas et al., 2018). Several plant species are capable of developing tolerance to this contaminant, and their adaptation capacity mainly depends on plant species, and within each species, on the genotypes of either subspecies or cultivars (Garg and Singla, 2011). A significant number of comprehensive reviews dealing with the interaction of As with higher plants are available (Zhao et al., 2009; Verbruggen et al., 2009; Garg and Singla, 2011; Chandrakar et al., 2016; Abbas et al., 2018). Some reviews focused on the accumulation of arsenic in rice, due to its relevance as a staple crop and its reported ability to accumulate this metalloid in grains (Lindsay and Maathuis, 2017; Chen et al., 2017a; Suriyagoda et al., 2018). Others have paid, instead, particular attention to the physico-chemical behavior of As in soil (Fendorf et al., 2010; Pigna et al., 2015; Strawn, 2018), its physiological impact on higher plants (Finnegan and

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https://doi.org/10.1016/j.ecoenv.2019.109701
Received 2 August 2019; Received in revised form 18 September 2019; Accepted 19 September 2019
Available online xxx
0147-6513/© 2019.

Chen, 2012; Chandrakar et al., 2016), and the mechanisms underlying its accumulation in higher plants (Farooq et al., 2016; Abbas et al., 2018). The present survey, instead, is intended to provide a systematic and critical description of the technical measures aimed either at counteracting or mitigating As accumulation in crops other than rice. The agronomic management of rice, in fact, generally involves periodic flooding conditions (Suriyagoda et al., 2018) while that of the vast majority of the other crops takes place under non-saturated soil conditions with ensuing differences in both mobility and speciation of this metalloid in soil (Pigna et al., 2015).

Several measures are currently available to mitigate metal (loid) levels in crops, and they can be divided into two main blocks (Edelstein and Ben-Hur, 2018). The first one includes plant-oriented techniques, such as genetic modifications, grafting of plants onto appropriate rootstocks and mycorrhization. The second block encompasses indirect techniques acting on the contaminated source, such as soil amendment with either inorganic and organic additives, and the treatment of irrigation water. However, for the sake of brevity, the vast subject of soil remediation techniques will not be taken into consideration in the present review for two main reasons. First, the topic has been faced thoroughly by very comprehensive reviews (Wang and Mulligan, 2006a; Butcher, 2009; Sarkar and Paul, 2016; Hanus-Fajerska and Kozminska, 2016). Second, and more importantly, the implementation of soil remediation techniques requires generally the set-aside of the treated soil until the achievement of clean-up goals. Consequently, this survey is limited only to those agronomic practices, the implementation of which is compatible with the continuation of cultivation, such as application of amendments, fertilization, and the treatment of irrigation water.

2. Impact of arsenic on human health

In the last decades, the ubiquitous presence of As in the environment has aroused increasing concern in both the scientific community and public authorities. Fig. 1 shows the principal sources of human exposure to As. The International Agency for Research on Cancer (IARC) has classified arsenic and its inorganic compounds as a Type I carcinogen for humans since a large body of evidence derived from epidemiological studies has been made available. In most mammals, including humans, the arsenic taken up by ingestion is rapidly absorbed in the gastrointestinal tract, and it is then conveyed through the circulatory system to organs and tissues (Abdul et al., 2015).

The liver, kidneys, heart, and lungs are typical targets of As accumulation. Its oxidation state mostly determines the mechanism of absorption of As at the cellular level. As(III) can enter the cells through aquaglyceroporins (Liu, 2010). At physiological pH, As(V), instead, behaves similarly to phosphate entering the cell presumably through phosphate-specific carriers or non-specific anionic carriers. Most mammals metabolize the inorganic forms of As through reductive and methylation mechanisms, and both kinds of reactions take place mostly at the hepatic level. Redox reactions involve arsenate reductase, glutathione-S-transferase omega 1 (GSTO1), and thiols (R–SH) as the electron donors. Among inorganic forms of arsenic, As(III), besides being more water-soluble is around 60-fold more toxic than As(V) due to its ability to react with thiol groups of cysteine residues in functional proteins thus leading to their deactivation (Abbas et al., 2018). At present, the mechanism of carcinogenesis induced by this element is not yet fully elucidated, but it is thought that it may involve oxidative stress, genotoxicity, inhibition of DNA repair and alterations in signal transduction or DNA methylation (Tchounwou et al., 2003). However, a very recent review collected a body of evidence that direct interaction of inorganic forms of arsenic with DNA does not occur, thus actively supporting a non-genotoxic mode of action (Cohen et al., 2019). Epidemiological studies have shown a close correlation between the presence of inorganic As in drinking water and the risk of developing cancer in skin, lung, bladder, and kidney (Halder et al., 2012; Karagas et al., 2015; Thomas, 2015). In addition to these tumoral diseases, prolonged As exposure might lead to neurotoxic conditions, glucose metabolism disorders and cardiovascular diseases; moreover, due to the ability of the As to overcome the placental barrier, damage to the fetus and abnormal growth of the newborn have also been reported (Abdul et al., 2015).

In 1993, as a consequence of the evident health problems associated with As contamination, the World Health Organization (WHO) lowered its limit value for the drinking water from 50 to 10 $\mu g\, L^{-1}$. With the 98/83/CE directive concerning the quality of the water destined to human consumption, the European Union adhered to these guidelines.

3. Chemistry of arsenic and occurrence in the environment

The joint action of natural and anthropic factors leads to either localized or widespread contamination. Arsenic is the main constituent of around 200 minerals, 60% of which are arsenates, 20% sulfates and the remaining arsenites, oxides, silicates and elemental As (Smedley and Kinniburgh, 2002). The most common As-containing minerals are arsenopyrite (FeAsS), realgar (As_4S_4), orpiment (As_2S_3) and enargite (Cu_3AsS_4) where the metalloid is associated with sulfur. Relevant concentrations of As are also found in other minerals, such as pyrite (FeS_2), galena (PbS), chalcopyrite ($CuFeS_2$) and marcasite (FeS_2), and (hydro)oxides derived from chemical alteration of primary sulfides. These minerals subjected to the "weathering" process release As in soluble form with ensuing contamination of groundwater and water wells. The environmental impact associated with this toxicant derives from its high mobility. Within this frame, areas characterized by hydrothermal phenomena assume particular relevance as a consequence of the over-exploitation of deep aquifers leading to "de novo" mobilization of some elements including As (Pallottino et al., 2018). Some As-containing compounds

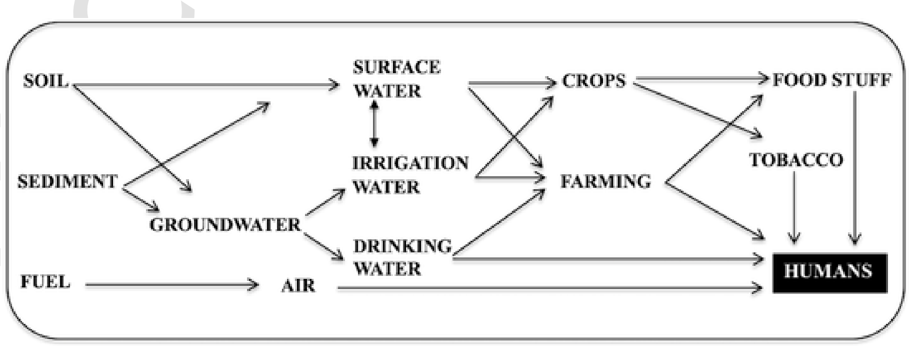

Fig. 1. Primary sources of arsenic exposure for humans.

are volatile, and this implies that the biogeochemical cycle of this element involves a relevant flux to the atmosphere where it is mainly found as As_2O_3 in the atmospheric dust (European Food Safety Authority, 2009). Studies focused on As flows have estimated that its annual emissions, arising from anthropic activities, can range from 52,000 to 112,0000 tons (Liao et al., 2005). The primary natural sources of atmospheric As derive from soil erosion, volcanic emissions (3000 tons per year) and the release of methylated arsines by microorganisms (20000 tons per year). Arsenic occurs in the environment, mostly in the trivalent and pentavalent oxidation states, that are found both in inorganic compounds and organic compounds, also including sugar and lipid derivatives (Fig. 2). Arsenate (AsO_4^{3-}) and arsenite (AsO_3^{3-}) anions are the most soluble and recurring inorganic forms found in water and soil; under highly reducing conditions, such as in groundwater and capillary fringe, the latter is the prevailing species, while arsenates are dominant under conditions of greater oxygenation, such as in the vadose and surface and marine waters (Fendorf et al., 2010). Monomethylarsonic (MMA) and dimethylarsinic acids (DMA) are typically organic compounds containing As(V) (Fig. 2). Trivalent As, instead, is typically found in mono-methylated species, such as monomethylarsonose acid [MMA (III)], and dimethylated ones, such as dimethylarsinous acid [DMA (III)]. More than 50 As-containing organic compounds have been identified, most of which found only in traces (European Food Safety Authority, 2009), and mainly represented by arsenobetaine, arsenocholine, arsenosugars, and arsenolipids.

The concentrations of the different forms of As in soil and their mobilities in the water-soil-plant system are affected by the inherent physico-chemical and biochemical properties of the soil itself, such as redox potential, pH, texture, presence of exchangeable ions, acting as As competitors, and, last but not least, biological activity and organic matter content (Pigna et al., 2015; Sarkar and Paul, 2016; Stazi et al., 2018). In soil, the bioavailable amounts of As are typically lower than its total content since the metalloid adsorbed on soil colloids tends to form, over time, increasingly stable surface complexes, which can either penetrate micropores or form precipitates with Fe and Al becoming increasingly less desorbed and bioavailable (Pigna et al., 2015). Although the mechanisms of adsorption of the inorganic forms of As on the surfaces of the mineral colloids in soil have been thoroughly investigated, the bioavailability of the metalloid depends markedly on the soil-water-plant system (Bolan et al., 2013; Abbas et al., 2018). Within this frame, the soil microbiota can affect both concentration and speciation of arsenic in the soil-plant system significantly through its ability to bring about the mutual inter-conversion of As(III) to As(V), and to volatilize the metalloid (Khalid et al., 2017; Crognale et al., 2017).

Maximum permissible limits (MPL) of arsenic for agricultural soils are variable depending on the country. To exemplify, in the majority of western countries, 20 mg As kg^{-1} is the maximum while in China, an MPL value up to 30 mg As kg^{-1} is accepted (Madeira et al., 2012).

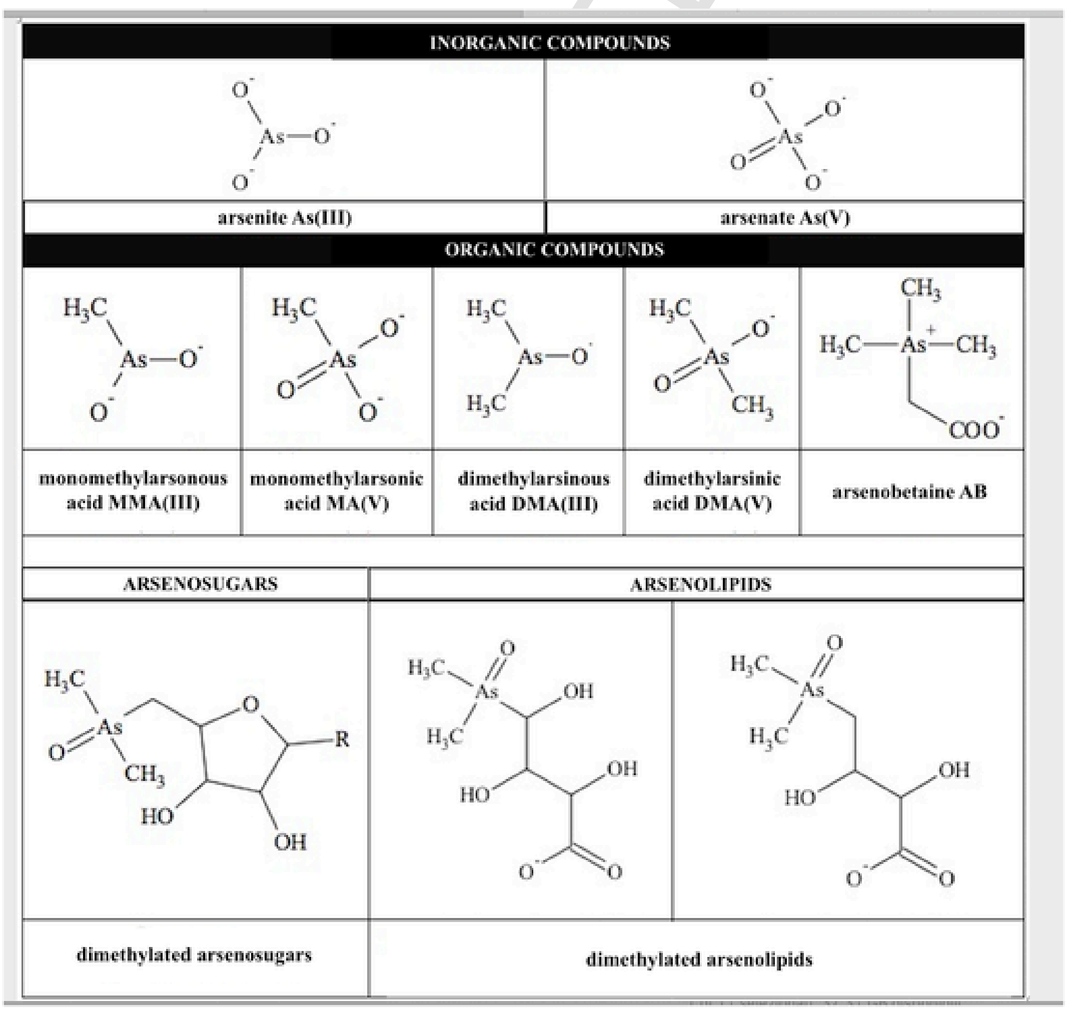

Fig. 2. Chemical structures of the main arsenic-containing inorganic and organic compounds detected in the biosphere.

3.1. Arsenic in higher plants: uptake, transport and accumulation mechanisms

The arsenic availability in soils is generally low, due to its strong adsorption on Fe, Mn and Al (hydro)oxides and clays (Mandal and Suzuki, 2002; Huang et al., 2006). The use of a variety of weak or mild extractants such as 0.01 M $CaCl_2$ or 0.05 M $(NH_4)_2SO_4$ (Száková et al., 2005) and 0.4 M acetic acid (Baroni et al., 2004) showed that the amounts of available As in soil ranged from 0.3 to 1.8% with respect to its total content. Due to the relative low As availability in soil, its concentrations in plant tissues are also low and reported to range from less than 10 to about 5000 $\mu g\,kg^{-1}$ on a dry matter basis (Mandal and Suzuki, 2002). In some areas affected by anthropic activities, the concentration of As can markedly exceed the above range. To exemplify, the As concentrations of crops collected from a former As smelter in the UK ranged between 80 and 21300 $\mu g\,kg^{-1}$ dry matter (Warren et al., 2003). The phytoavailable As is first taken up by the root system and then transferred and differentially accumulated in different organs of the plant (Kabata-Pendias, 2010). Fig. 3 summarizes the primary biochemical systems involved in the interaction of the plant with the metalloid. Maurel et al. (2008) reported that As(III) uptake by the plant involves a passive transport system mediated by aquaporins (noduline26-like, NIPs). These intrinsic membrane proteins are characterized by a typical motif of three amino acids (Asparagine-Proline-Alanine), forming the channel through which ions and solutes pass, and an aromatic peptide loop which constitutes the selective filter to the passage of the molecules in the channel.

As already mentioned, due to its structural similarity, phosphate competes with arsenate for the same transport system involving a proton co-transport with a stoichiometric ratio of $2H^+$: $H_2PO_4^-/H_2AsO_4^-$ (Zhao et al., 2009). High (PHT1) and medium affinity phosphate transporters were identified as the specific carriers involved in the influx of the vast majority of the arsenate (Catarecha et al., 2007). Once absorbed by the roots, the arsenate is reduced enzymatically to arsenite with the concomitant oxidation of glutathione (GSH) to glutathione disulfide (GSSG) in a reaction brought about by arsenate reductase (Verbruggen et al., 2009). The arsenite thus formed can undergo a variety of fates including (i) storage inside the vacuoles (ii) volatilization (iii) efflux through specialized transport systems, and (iv) transport to the aerial part. The primary defense mechanism from As(III) involves its binding by phytochelatins (PC) that are low molecular weight proteins rich in cysteine residues and belonging to the III class of the family of metallothioneins. The thiol groups of the cysteine residues in the polypeptide are capable of binding metal (loid)s, thus avoiding their harmful interaction with the cell components.

The fate of the As(III)-PC complexes involves their internalization within the vacuole which is mediated by trans-membrane proteins of the tonoplast, named ABC transporters (ATP-binding cassette transporters) (Song et al., 2010).

An additional response mechanism of plants to As(III) involves its volatilization after methylation. Xu et al., (2007) found some methylated forms of As in cucumber (*Cucumis sativus*), and tomato (*Lycopersicon esculentum*) and reported that their relative abundances were lower than 4% as compared to total accumulated arsenic. To date, however, and as opposed to bacteria and fungi, the volatilization mechanism has not been fully clarified in higher plants (Ye et al., 2012; Mestrot et al., 2013). Lastly, although the root systems of several plant species were capable of a substantial As(III) efflux, it is not clear yet whether this phenomenon contributes significantly to the detoxification mechanisms put in place by plants (Farooq et al., 2016). NIPs, a subclass of aquaporins, in addition to their primary function of silicon transport, are involved the outflow of arsenite (Briat, 2010). Moreover, Zhao at al., (2010) provided evidence that Lsi1, in rice, is permeable to arsenite from both directions and that the direction of flow is dependent on the concentration gradient.

Concerning the fate, instead, of the residual As(V) pool that has not undergone catalytic reduction, Xu et al. (2007) suggested that anionic channels might be involved in its release in the external medium following the same pathway of the phosphate. The inorganic arsenic pool that does not undergo the previously mentioned metabolic pathways can be transported to the aerial part through the

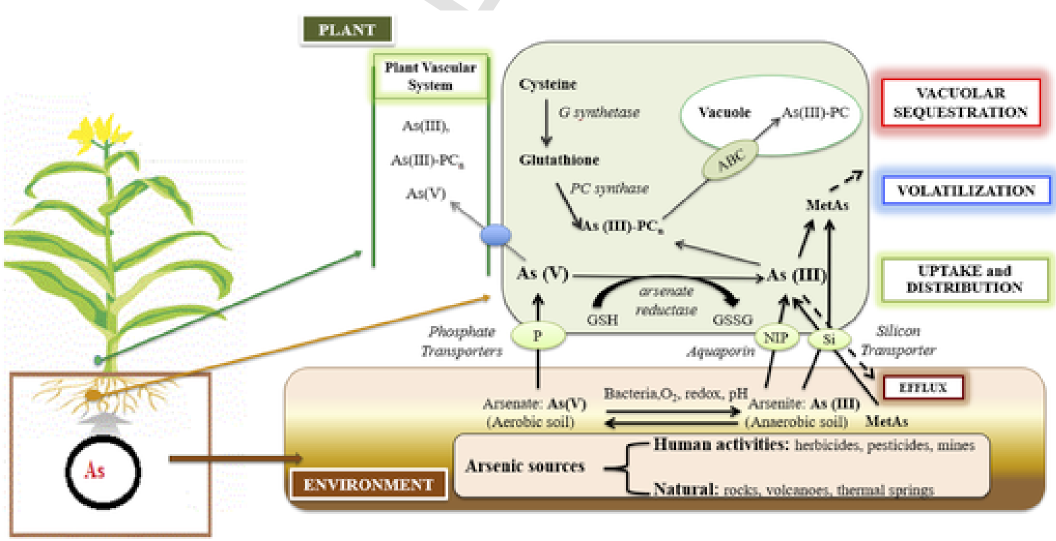

Fig. 3. Arsenic cycle in the environment and its fate in plants (Adapted from Briat, 2010). Equilibrium between arsenate and arsenite in the circulating solution of soil is mainly governed by redox conditions. Uptake of arsenate and arsenite by roots involves phosphate transporters (P) and a subclass of aquaporins (NIP), also involved in silicon (Si) transport, respectively. These types of transporters are also responsible for the distribution of As between plant's organs. Once inside the plant, As(V) is reduced to As(III) by arsenate reductase with the concomitant oxidation of glutathione (GSH) to glutathione disulfide (GSSG). The fates of the As(III) thus formed can be (i) efflux through root Si transporters, (ii) methylation with the ensuing formation of MetAs and (iii) confinement within the vacuole after its binding to phytochelatins (PCs). The transport of the PC–As(III) complexes to the vacuole involves members of a subclass of ATP binding cassette (ABC) transporters. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

xylem. The xylematic transport of As is essential for the distribution and accumulation of the metalloid in the above-ground plant biomass. It takes place thanks to the water flow created by transpiration current, mediated, under particular conditions, by membrane transport proteins (Lindsay and Maathuis, 2017). Zhao et al., (2009) have shown that As(III) is the predominant form in xylematic tissue (from 60 to 100% of total As). In rice, a specific silicon transporter, referred to as Lsi2, mediates the transfer of As(III) from the root cells to the xylem (Ma et al., 2008). In plants other than rice, a recent study reported that Natural Resistance-Associated Macrophage Protein (NRAMP) might mediate the loading of As(III) in the xylem and its ensuing accumulation in the aerial part (Tiwari et al., 2014). The transport of As(V) to the xylem, instead, seems to involve the same pathway of phosphate, as it occurs in the root cells (Farooq et al., 2016).

In the leaves, As(V) can be reduced to As(III) through enzymatic and non-enzymatic transformations both involving a concomitant GSH oxidation. The As(III), once formed in this site, may undergo methylation processes by the inducible enzyme arsenite methyltransferase (Duan, 2005). Limited information exists, however, concerning the prevalent forms of As in the phloem and the transporters involved in its loading to the sieve tube elements and its subsequent unloading to seeds and fruits. Duan et al., (2016) hypothesized that inositol transporters might be involved in the loading of the arsenite into the phloem, which is a fundamental step regulating the accumulation of arsenic in the seeds.

4. Occurrence and bioavailability of arsenic in edible crops and foods thereof derived

Some crops are reportedly capable of accumulating higher levels of As than others (Warren et al., 2003; Huang et al., 2006; Zhang et al., 2009) and Table 1 shows the As concentration ranges found in a variety of vegetables, fruits, and spices.

To quantify the As-accumulation capacity in plants, the soil-to-plant transfer factors (TF), also referred to as bioaccumulation factor, and either based on total or available As, as shown in Equations (1) and (2), respectively, have been used.

$$TF_{tot} = \frac{As_{ep}}{As_{tot}} \tag{1}$$

$$TF_{av} = \frac{As_{ep}}{As_{av}} \tag{2}$$

where As_{tot} and As_{av} represent the total and available contents of arsenic in soil, respectively, and As_{ep} the content of arsenic in the edible part of the plant.

The As_{ep} in a given crop, in addition to depending on the As_{av} in the soil, also depends on the ability of that crop to perform its uptake and the subsequent translocation to the target organs. Since plant roots can retain significant amounts of arsenic, tubers, edible roots, and bulbs are good candidates to perform its accumulation (Zhang et al., 2009). Potatoes (Moyano et al., 2009) and radishes (Warren et al., 2003), and bulbs, such as garlic and onions (Huang et al., 2006; Zhao et al., 2009), exhibited high levels of arsenic when grown in As-contaminated soils. Huang et al. (2006) found that As_{ep} correlated better with As_{av} than As_{tot}; as a consequence, the TF_{av} was used to compare the accumulation ability of various horticultural crops leading to the following decreasing rank: radish > water spinach > celery > onion > leaf mustard > fragrant-flowered garlic > Chinese cabbage > lettuce > garlic > cowpea > cauliflower > bottle gourd > towel gourd > eggplant. In the same work, the TF_{av} values of the crops under study ranged from 0.001 to 0.12. Several other sequences, albeit based on TF_{tot}, are available for horticultural species and report a high As-accumulating

Table 1
Concentration ranges of total arsenic found in fruits, vegetables and spices listed in alphabetical order.

Crop	Scientific name	As concentration range [a] (mg kg $^{-1}$)	References
Banana	*Musa paradisiaca* L.	0.086–0.67	Islam et al. (2017)
	Musa sapientum L.	0.011–0.014	Wang et al. (2013)
Bean	*Phaseolus vulgaris* L.	0.22–0.49 f.w.‡	Islam et al. (2017)
		0.005–0.223	Ciminelli et al. (2017)
		0.01–0.28	Bhattacharya et al. (2010)
Cabbage	*Brassica oleracea* L. var. *capitata* L.	0.11–0.3	Bhattacharya et al. (2010)
		0.001–0.016	Huang et al. (2006)
Cauliflower	*Brassica oleracea* var. *botrytis* L.	0.14–0.48	Bhattacharya et al. (2010)
Carrot	*Daucus carota* L.	0.15–0.44 f.w.‡	Islam et al. (2017)
		0.035–0.038	Wang et al. (2013)
		0.058–0.135	Arain et al. (2009)
Chili	*Capsicum annuum* L.	0.15–0.38	Islam et al. (2017)
Coriander	*Coriandrum sativum* L.	0.18–0.98	Arain et al. (2009)
Cucumber	*Citrullus lanatus* Thunb	0.011–0.074	Wang et al. (2013)
Eggplant	*Solanum melongena* L	0.091–0.27	Islam et al. (2017)
		0.007–0.012	Wang et al. (2013)
		0.35–0.57	Arain et al. (2009)
		0.01–0.41	Bhattacharya et al. (2010)
Garlic	*Allium sativum* L.	0.17–0.79	Bhattacharya et al. (2010)
		0.006–0.159	Huang et al. (2006)
Lettuce	*Lactuca sativa* L.	0.002–0.105	Huang et al. (2006)
Lemon	*Citrus limon* L.	0–0.050	Bhattacharya et al. (2010)
Lentil	*Lens culinaris* L.	0.17–0.49	Islam et al. (2017)
Mango	*Mangifera indica* L.	0.15–0.29	Islam et al. (2017)
Onion	*Allium cepa* L.	0.17–0.49	Islam et al. (2017)
		0.018–0.048	Arain et al. (2009)
		0.11–0.25	Bhattacharya et al. (2010)
		0.005–0.157	Huang et al. (2006)
Papaya	*Carica papaya* L.	0.17–0.62	Bhattacharya et al. (2010
Peppermint	*Mentha* × *piperita* L.	0.45–1.20	Arain et al. (2009)

Table 1 (*Continued*)

Crop	Scientific name	As concentration range[a] (mg kg $^{-1}$)	References
Potato	*Solanum tuberosum* L.	0.17–0.47	Islam et al. (2017);
		0.19–1.02	Bhattacharya et al. (2010)
		0.056–0.256	Arain et al. (2009)
Pumpkin	*Cucurbita pepo* L.	0.04–0.36	Bhattacharya et al. (2010)
Radish	*Raphanus raphanistrum* L. subsp. *sativus* (Schmalh*)*	0.1–0.66	Bhattacharya et al. (2010)
Spinach	*Spinacia oleracea.* L.	0.214–0.9	Arain et al. (2009)
		0.24–0.35	Halder et al. (2012)
		0.17–0.79	Bhattacharya et al. (2010)
Tomato	*Lycopersicon esculentum* Mill.	0.14–0.53	Islam et al. (2017)
		0.03–0.29	Bhattacharya et al. (2010)

[a] Unless stated otherwise, data are referred to dry weight; ‡f. w., fresh weight.

Table 2
Average and maximum values of total arsenic, expressed on the dry matter basis, and found in some plant-derived foods (European Food Safety Authority, 2009).

Matrix	Total As (mg kg $^{-1}$)		Maximum value found in:
	Average value	Maximum value	
Cereal grains excluding rice	0.02	5.66	
Grain rice	0.14	1.18	
Sugar, confectionery and chocolate	0.01	1.07	Honey
Vegetables fats and oils	0.01	0.1	
Starchy roots and potatoes	0.003	0.23	
Fruits	0.006	2.20	Apricot (fresh weight)
Coffee, tea, cocoa	0.049	1.44	Tea and other infusion
Mushrooms	0.06	19.20	
Brassicaceae	0.03	0.15	
Legumes	0.01	0.34	
Walnuts	0.01	0.44	
Alcoholic beverages	0.01	0.69	sparkling wine and wine produced with fermented fruit
Spices	0.09	2.42	
Freeze-dried vegetables	0.13	1.50	
Seaweed	30.87	236.00	

propensity of some crops, such as radish, potato and cauliflower (Alam et al., 2003; Warren et al., 2003).

The typical TF_{tot} for As reported by Warren et al. (2003) ranged from 0.0007 to 0.032 and radish tubers and calabrese leaves had the highest values of this parameter. Those reported by Alam et al. (2003) from a heavily As-contaminated village in Bangladesh for potato, ash gourd, green papaya, ghotkol, and snake gourd were 0.006, 0.006, 0.030, 0.034 and 0.038, respectively. The increased accumulation of arsenic in edible crops also derives from the use of As-contaminated groundwater for irrigation purposes; for instance, de la Fuente et al. (2010) found that the transfer factors of As in several crops largely exceeded those reported in the literature and this was also due to the high mobility of the metalloid enabled by the sandy texture of the soils under study. The same investigation reported that inorganic As contributed with very significant proportions (49–100%) to the total As taken up by the plant in a variety of horticultural crops in agreement with Díaz et al. (2004). Several studies point out that concentrations of As in the edible parts of leafy vegetables are generally higher than those found in non-leafy vegetables (e.g., eggplant, cowpea, towel gourd) (Liao et al., 2005; Huang et al., 2006).

The European Food Safety Authority (2009) documented that the content of arsenic varies significantly in different products of plant origin, as shown in Table 2. The scientific opinion expressed by the EFSA's group of experts on contaminants in the food chain (CONTAM group), in relation to the presence of As in food, highlighted that heavy consumers of rice in Europe and children under the age of 3 are the most exposed subjects to the potentially harmful effects of As. Generally, the potential health risks associated with chronic exposure to single or multiple inorganic pollutants due to the consumption of contaminated food are estimated on the basis of the daily intake rate (DIR), shown in Equation (3) and expressed as μg pollutant day $^{-1}$ kg $^{-1}$ body weight (Roba et al., 2016):

$$\mathrm{DIR} = \frac{IR \cdot C}{BW} \qquad (3)$$

where IR, C and BW are the ingestion rate, concentration of the pollutant in food and mean body weight of an adult, respectively. On this basis, the estimates of EFSA indicate that the inorganic arsenic exposures, derived from water and food, in 19 European countries could vary in intervals (depending on the type of cancer or pathology) from 0.13 to 0.56 μg kg $^{-1}$ of body weight per day for average consumers, and from 0.37 to 1.22 μg kg $^{-1}$ of body weight per day for consumers placed on the ninety-fifth percentile (European Food Safety Authority, 2009).

While the determination of the total arsenic concentration in the food of concern can enable the estimation of the exposure doses (intake), the amount of the metalloid, that is taken up and reaches the systemic circulation, referred to as the bioavailable fraction, is a more valuable indicator of potential toxicity and ensuing health hazard (Juhasz et al., 2008). The bioavailability of arsenic to humans also depends on its speciation in the contaminated food, dietary composition, and the nutritional status of the individual (Yager et al., 2015). Thus, the determination of the chemical forms of arsenic in each food is more important than the dosage of its total content to assess health risk in humans derived from diet (Cubadda et al., 2017). As already mentioned, the inorganic forms of arsenic exhibit higher toxicity than its methylated compounds, such as monomethylarsonic acid (MA) and dimethylarsinic acid (DMA) (Michalski et al., 2012); moreover, organo-arsenicals, including arsenobetaine, and arsenocholine, occurring primarily in seafood, have low or negligible toxicity (Chávez-Capilla et al., 2016). Several studies focusing on multi-pathway exposures to arsenic have demonstrated that diet is the primary contributor to total and inorganic arsenic exposure only when the concentrations of the metalloid in potable water are not high (Schoof et al., 1999; Kurzius-Spencer et al., 2014). In a market basket survey, conducted in the USA, the highest values of inorganic arsenic were found in raw rice (74 ng g $^{-1}$), flour (11 ng g $^{-1}$), grape juice (9 ng g $^{-1}$) and cooked spinach (6 ng g $^{-1}$) (Schoof et al., 1999).

The oral bioavailability of arsenic can be investigated by using several *in vivo* models, including rodents, juvenile swine, and primates (Moreda-Piñeiro et al., 2011). Downstream of the intake, the gastrointestinal tract of laboratory animals promptly absorbs water-soluble As compounds, and then the concentrations of arsenic in blood and organs or its excreted amounts in urine or feces are used to estimate the fraction of the dose reaching the systemic circulation. However, with the notable exception of rice (Laparra et al., 2005; Juhasz et al., 2006; He and Zheng, 2010), a paucity of information is currently available on the bioavailability of As in other edible crops (Juhasz et al., 2008; Yager et al., 2015), despite the documented ability of a variety of vegetables to accumulate As in their edible parts. In particular, Juhasz et al., (2008) evaluated the bioavailability in a variety of crops, including lettuce (*Lactuca sativa* L.), chard (*Beta vulgaris* L.), radish (*Rhapanus sativus* L.), and mung beans (*Vigna radiata* L.), grown under greenhouse conditions and irrigated with arsenate-contaminated water; the bioavailability of arsenic amounted to 52 ± 18% and 50 ± 13%, for chard and lettuce, respectively; radish, and mung beans, instead, exhibited considerably higher bioavailability values (77 ± 20% and 98 ± 23%, respectively).

The scarce availableness of data on bioavailability in food is mainly due to the limitations of *in vivo* approaches primarily attributable to the complexity of the procedures and economic and ethical reasons (Yager et al., 2015). Alternative approaches to determine the chemical risk to humans, derived from dietary intake, include *in vitro* physiologically-based extraction tests (PBET), aimed at determining the bioaccessibility, that is assumed to represent the maximum fraction of a dose available for intestinal absorption (Intawongse and Dean, 2006; Yager et al., 2015). *In vitro* methods are designed to simulate the pH of the fasting state in a young child, and these conditions have been found to lead to higher bioaccessibility values for many metal (loid)s and thus are considered a more conservative approach (Moreda-Piñeiro et al., 2011). By using a PBET-based approach, Pizarro et al. (2017) found that the bioaccessibility value of As for quinoa (*Chenopodium quinoa* Willd.) was around 40% while those in carrots (*Daucus carota* subsp. sativus Hoffm.) and beets (*Beta vulgaris* L.) were very close to 100%; thus, based on annual intake of these vegetables and their related total As concentrations and moisture contents, quinoa was deemed to be the vegetable with the lowest toxicological implications. In addition to depending on the type of food and the experimental conditions adopted in the test (Moreda-Piñeiro et al., 2011), both bioavailability and bioaccessibility can be affected by the processing and preparation (*e.g.*, milling, cooking, baking, steaming, etc) of the food itself (Laparra et al., 2005; Juhasz et al., 2008; Hu et al., 2019; Cubadda et al., 2017).

4.1. Reducing arsenic transfer to edible plant tissues

The presence of arsenic in the environment represents a severe menace to the agricultural activity due to the potential contamination of the edible products thereof derived. Unlike drinking water, the As content of which can be quantified and subsequently minimized, the contamination of agricultural products has more complicated and not always governable causes.

4.2. Use of inorganic and/or organic amendments

The main determinants for the concentrations of arsenic in crops are the metalloid's mobility in soil and the ability of the plant to perform its uptake and subsequent translocation to the target organs. Adsorption-desorption reactions govern largely arsenic mobility in the soil even though other processes, such as precipitation and volatilization, can take place (Pigna et al., 2015). Therefore, the application of low-cost additives aimed at reducing As mobility in the soil can reduce its transfer to the food chain albeit their efficacy can be markedly affected by different properties of soils such as, for instance, pH, texture, and concentrations of competing ions (Wang and Mulligan, 2006a). Different materials, such as iron, aluminum, and manganese (hydro)oxides and clay minerals are efficient As adsorbents (de la Fuente et al., 2010). Among them, the attention has been mainly focused on iron-based ones due to the efficacy of iron (hydro)oxides in retaining this metalloid (Warren et al., 2003; Hartley and Lepp, 2008). In a field-scale experiment, conducted in a highly As-contaminated soil (748 mg As kg^{-1} soil), application of ferrous sulfate in solution to the topsoil, providing 0.2% Fe oxides, reduced As plant uptake by a mean of 22% using a variety of horticultural crops (i.e., calabrese, cauliflower, lettuce, potato, beetroot and radish) (Warren et al., 2003). In this study, Calabrese leaves, cauliflower, and radish skin exhibited the most relevant reductions due to the amendment since their TF_{tot} values were half of those found in the non-amended control. In another study, the application of lamination slags, iron-based byproducts of the hot rolling of steel, to alkaline and sandy soils exerted somewhat limited impact on As mobility and did not modify the bioaccumulation factor in a variety of horticultural crops as compared to the non-amended control (de la Fuente et al., 2010); the authors suggested that the high concentration of available P, the low clay content and the alkaline conditions of the tested soils limited As adsorption on the surfaces of iron oxides of lamination slags (de la Fuente et al., 2010). Among four iron-bearing additives, goethite (α-FeOOH) (crystallized iron oxide), applied at 1% to a variety of As-contaminated soils with different origins and textural properties, was the most effective since it attenuated phytotoxic effects and led to the lowest As content in shoots of tomato and spinach (Hartley and Lepp, 2008). In another study, the application of goethite at 3 g kg^{-1} soil markedly decreased the amount of extractable arsenic and reduced the root to shoot translocation factor in parsley (Madeira et al., 2012). Among other metallurgical byproducts, red mud, derived from the chemical processing of bauxite and its derivatives, has also been shown to be a valuable soil amendment due to its capacity of reducing the amounts of As_{av} (Ahmaruzzaman, 2011) and its uptake by plants (Pardo et al., 2017). Hua et al. (2017) suggested that the efficacy of the red mud in reducing the mobility of arsenic is due to its high content in Fe and Al (hydro)oxides (*i.e.*, boehmite, cancrinite, and gibbsite), which are the primary components involved in the immobilization of metal (loid)s. In a recent study, three Fe-oxide-rich materials (i.e., Bayoxide®, lamination slag, and red mud), were assessed comparatively for their abilities to attenuate the impact due to the use of As-rich irrigation water in a non-contaminated agricultural soil (Arco-Lázaro et al., 2018). Among the tested amendments, only Bayoxide®, a commercial iron oxide formulation, was able to reduce As_{av} in the soil; however, none of them was able to mitigate the As uptake by *Lactuca sativa* used as the test plant (Arco-Lázaro et al., 2018).

The investigation on the impact of organic amendments on the mobility of arsenic in soil has led to conflicting results. On the one hand, it has been reported that such amendments led to increased As mobility with ensuing higher plant uptake of the metalloid (Renella et al., 2007; Hartley and Lepp, 2008; Clemente et al., 2010). On the other hand, it was found that available As was stabilized upon the application of organic matter to soil (Gadepalle et al., 2007). These contrasting results might be due to different degrees of organic matter stabilization which characterized those amendments. Moreover, pH conditions should not be neglected as observed by de la Fuente et al. (2010) who applied compost to alkaline soils. These investigators suggested that irrespective of the type of organic matter and the presence of competing ions, the pH might counteract the potential beneficial effects of composts on the reduction of As mobility in soils (de la Fuente et al., 2010). In fact, as the soil pH increases, hydroxyl ions replace arsenic oxyanions on the soil sorption sites leading to their subsequent release into solution (Carbonell-Barrachina et al., 1999). Moreover, under acidic conditions, organic matter is capable of forming surface complexes with iron hydroxides thus competing with arsenic for the same adsorption sites; this effect leads to the release of arsenic to soil solution (Wang and Mulligan, 2006b). The impact of the organic matter addition is also affected by the type of crop; Madeira et al. (2012) found that the addition of an olive-mill waste compost to a highly contaminated soil significantly reduced the As concentrations in tomato fruit while the levels of the pollutant in parsley shoot were not affected at all as compared to the non-amended counterpart. Among other organic-based amendments, biochar has been shown to reduce the bioavailability of metal (loid)s (Oh and Yoon, 2016; Ippolito et al., 2017) and to enable successful revegetation of contaminated areas (Park et al., 2011). Biochar is the byproduct of a variety of thermochemical processes, including slow or fast pyrolysis, torrefaction, hydrothermal carbonization, and gasification; it can be obtained from several wastes, such as crop residues, weeds, wood sawdust, litter, and municipal solid waste. With specific regard to arsenic, Beesley et al., (2010) found that soil amendment with biochar led to an increase of the water-leachable fraction of the metalloid. In a subsequent study, the same group reported that although the addition of biochar resulted in an increased pore water concentration of As, its transfer to tomato plant tissues was lower than that found in the non-amended soil (Beesley et al., 2013). At the same time, other studies observed that the addition of biochar to As-contaminated soils did not reduce the As uptake by Miscanthus (*Miscanthus giganteus*) (Hartley et al., 2009) and maize (Namgay et al., 2010); however, these studies were conducted in alkaline soils, and this might have masked the effect of biochar amendment. In this respect, the liming effect of biochar is largely known, and the resulting pH increase has been shown to play a significant impact on arsenic mobility in soil (Hartley et al., 2009; Namgay et al., 2010; Beesley and Marmiroli, 2011). Gregory et al. (2014), in fact, reported that the application of biochar to acidic soils resulted in an increased concentration in ryegrass shoots as compared to the non-amended control; this effect was ascribed to an increase in soil alkalinity due to biochar amendment. In addition to this, some key properties of biochar, including pore structure, surface area, and adsorption properties, are known to be affected by the pyrolytic temperature and the type of feedstock composition (Vithanage et al., 2017). In high-temperature biochars, aliphatic moieties are readily transformed into aromatic rings with the ensuing generation of a graphene-like structure that, in turn, gives the material improved pore distribution and surface area (Ahmad et al., 2014). Biochars with a highly condensed aromatic ring structure exhibit generally a surface endowed with few functional groups, which are the main determinants for the adsorption capacity of biochar (Uchimiya et al., 2013). Low-temperature biochars with a low degree of aromaticity, instead, contain more adsorption sites for contaminants (Vithanage et al., 2017). Despite the conflicting results about the impact of biochar on arsenic mobility, there is general agreement regarding its capability of modifying the chemistry of arsenic in the soil. In addition to the aforementioned effect on soil pH, these modifications may be due to either a direct effect on the redox status of the soil or an indirect effect mediated by the soil microbiota which is generally stimulated by the presence of biochar (Joseph et al., 2010; Gregory et al., 2014; Strawn, 2018). Some studies provided evidence that increased microbial activity promoted change in arsenic speciation from arsenate to arsenite thus resulting in higher bioavailability to plants (Ruiz-Chancho et al., 2008; Bolan et al., 2012).

4.3. Possible interventions on irrigation water

The use of As-contaminated water for crop irrigation has increased As uptake from soils into plants for decades (Williams et al., 2006; Kahn et al., 2009). To date, however, and as opposed to drinking water, no regulation concerning As permissible limits in irrigation water has come into force. Background concentrations of arsenic in groundwater are in most countries less than $10\,\mu g\,L^{-1}$ (Chen et al., 2001) although values quoted in the literature show four orders of magnitude range (i.e., from 0.5 to $5000\,\mu g\,L^{-1}$) (Mandal and Suzuki, 2002). Groundwater exhibits high concentrations of arsenic in a variety of environments, including both oxidizing (under highly alkaline conditions) and reducing aquifers and in areas affected by geothermal, mining and industrial activity. Moreover, groundwater is the only water source available to many arid and semi-arid areas due to the dominance of dry conditions. In the Mexican states of Durango and Coahuila, concentrations up to 0.87 mg of As L^{-1} have been detected in groundwater (Pineda-Chacón and Alarcón-Herrera, 2016). The use of clean or purified irrigation water would be the most obvious approach; however, the exploitation of physico-chemical techniques is impractical from a techno-economic viewpoint. A sustainable option, which, however, implies periodical pumping of groundwater and its accumulation in treatment basins, might be represented by the phytofiltration, a range of techniques relying on plants/roots to perform water decontamination (Hanus-Fajerska and Kozminska, 2016). Aquatic, semi-aquatic, and terrestrial plants have been successfully used to perform arsenic removal from water (Haque et al., 2007). Two alternative strategies have pursued arsenic decontamination by this method, the former relying on plants requiring a support structure and the latter based on the use of plants that float on the surface of water bodies. The first approach relies on species, such as *Pteris vittata*, which is grown under hydroponic conditions in contaminated water (Malik et al., 2009). Huang et al. (2004) claimed that this species is capable of reducing As concentrations in a few hours. The second As-decontamination approach, instead, is based on the concomitant use of plants belonging to the genus *Lemna* and the macrophyte *Spirodela polyrhiza* (Sasmaz and Obek, 2009).

4.4. Fertilization

The knowledge of the processes of As mobility and transport in the plant-soil systems enables the application of fertilization techniques in different contamination scenarios aimed at mitigating the contamination of plants and, ultimately, of plant-derived agricultural products.

On the one hand, under reducing conditions, it is possible to decrease the phytoavailability of As(III) with the aid of silicon-based fertilizers and this technique is currently used for rice (Zhao et al., 2010). Rice fertilization with Si resulted in lower As accumulation in plants (Guo et al., 2008; Li et al., 2009) and was based on the evidence that As(III) is taken up by roots *via* water channels that also are involved in the absorption of boron and silicon (Ma et al., 2008). Although flooding is not mandatory for rice cultivation, it is conventionally used and thus very far from the cultivation of the vast majority of horticultural crops under soil's moisture conditions well below the water-holding capacity. For this reason, As(V) is by far the prevalent species, under unsaturated field conditions. Fertilization with P has been shown to mobilize arsenate in soil, due to the ability of phosphate to perform its desorption from soil colloids (Fendorf et al., 2010).

As a consequence, several studies reported an increase in As accumulation in plant tissues of chickpea (Gunes et al., 2009) when P was applied. These results are clearly in contrast to those of Meharg and Macnair (1994) suggesting that high phosphate concentration in the soil favors uptake of phosphate rather than of arsenate since the high-affinity phosphate transporters bind preferentially the former oxyanion. Several other studies confirmed that the application of phosphorus-based fertilizers led to a reduction in the As plant levels (Khattak et al., 1991; Pigna et al., 2009).

4.5. Grafting

The grafting is a consolidated practice, mainly aimed at preventing plants from damage due to pathogens and soil-borne pests. However, recent studies claimed that grafting of vegetables could also improve their tolerance to heavy metals (Colla et al., 2013; Kumar et al., 2015; Savvas et al., 2010). Bergqvist et al., (2014) suggested that the success of this practice might be since the genotype of the rootstock affects both root structure and root exudates, which, in turn, govern the uptake of metals. With the only exception of chromium (Balal et al., 2017), the majority of studies regarded those toxic elements, such as lead, nickel, cadmium and copper, mainly present as cations in soil, as opposed to As, which occurs mainly as oxyanions. To date, there is a single study dealing with the arsenic uptake and its partitioning in grafted tomato plants (Stazi et al., 2016). In this study, regardless of the rootstock, As accumulation mainly took place in root, and its translocation to the shoot and fruits occurred to a minimal extent; however, both uptake and distribution of As in plant tissues were differentially affected by the type of rootstock; among them, the 'Maxifort' rootstock was more efficient than 'He-Man' and 'Caramba' at mitigating As uptake in roots even though this was associated with increased As accumulation in tomato fruits (Stazi et al., 2016). Anyhow, based on DIR values and current international guidelines (European Food Safety Authority, 2009) indicating a tolerability range for daily intake from 0.3 to $8\,\mu g\,kg^{-1}$ body weight, the tomato fruits from Maxifort-grafted plants did not accumulate hazardous levels of As.

4.6. Mycorrhization

Plant root-associated microorganisms are reportedly able to affect the availability of metal (loids) and their uptake by plants (Smith et al., 2010). Mycorrhizal fungi represent a significant component of the microbiota in the rhizosphere and can establish different associative forms with plants, referred to as ectomycorrhizas, arbuscular mycorrhizas (AM), orchid mycorrhizas and ericaceous mycorrhizas. Among them, AM fungal associations are the most widespread (Smith et al., 2010; Garg et al., 2015). Mycorrhization appears to be a promising approach to attenuate the As transfer from soil to plant taking into account that the majority of higher plant species (around 90%) can interact with mycorrhizal species (Chen et al., 2007; Smith et al., 2010). Plant tissues infected with mycorrhizae exhibited a higher P/As ratio than non-infected ones, and this gave the plants a higher tolerance to As (Smith et al., 2010). Some investigators claimed that the As content in mycorrhized plants was lower than non-infected counterparts and these results were ascribed either to a slower rate of root uptake of As (Yu et al., 2009) or a dilution effect from increased plant growth (Smith et al., 2010). As previously mentioned, mycorrhized plants show generally better growth than non-mycorrhized plants as a consequence of the enhanced nutrients uptake, which, in turn, is due to the expansion of the extra-radical mycelium of the AMFs beyond depletion zone (Spagnoletti et al., 2017).

Moreover, AM fungi block the As in their mycelial structures (intra-radical hyphae, arbuscules, and vesicles), hindering its translocation to the aerial parts of the plants (Smith et al., 2010). AM are also capable of reducing the As roots uptake through their known ability to modulate PHT1 transporters; as a consequence, the alternative mycorrhizal pathway replaces the direct path involved in P uptake (Christophersen et al., 2009). In addition to this, AM fungi are active producers of glomalin, an insoluble glycoprotein, endowed with metal (loid)-binding ability (Gonzalez-Chavez et al., 2004).

4.7. Genetic selection and transgenic plants

An ever-increasing body of evidence shows that it is possible to affect As tolerance and its accumulation in plants *via* genetic manipulations. However, the vast majority of efforts have been focused on rice, a crop the agronomic management of which is far from that of horticultural crops, and these results have been summarized in a comprehensive and recent review (Chen et al., 2017a). For this reason, the present survey does not take into consideration these rice-oriented studies. Although genetic techniques, relying on the introduction of heterologous genes or alteration of expression levels of existing genes, have been shown in several cases to increase As tolerance in plants other than rice, they have been seldom applied to edible crops (Gasic and Korban, 2007; Reisinger et al., 2008) and mostly regard *Arabidopsis thaliana* and *Nicotiana tabaccum*. However, this survey intends to mention which targets can be pursued by manipulating components involved in plant response to As, such as As(V) and As(III) plasma membrane and vacuolar transporters, enzymes, peptides, and transcription factors.

Plant uptake of As(III) and As(V) oxyanions takes place through aquaglyceroporins and phosphate transporters (PHTs), respectively; the other classes of As(III) transporters include plasmalemma intrinsic proteins (PIP) and tonoplast intrinsic proteins (TIP) (Kumari et al., 2018).

The expression in *A. thaliana* of *PvTIP4;1*, coding for a TIP transporter in *P. vittata*, resulted in a significant increase in As accumulation in transgenic lines albeit associated with enhanced susceptibility to As stress as compared to the wild type (WT) (He et al., 2016).

A. thaliana transgenic plants heterologously expressing *OsNRAMP1*, coding for an As(III) transporter in rice, exhibited enhanced tolerance to As(III) and higher biomass production than the WT (Tiwari et al., 2014). The As-reducing enzyme HAC1/ATQ1, located in the root epidermis and root hair cells, was identified and found to play a pivotal function in the modulation of the resistance to arsenate (Chao et al., 2014; Sanchez-Bermejo et al., 2014) and the loss of function of *HAC1* was found to lead to reduced As(III) efflux and the over-accumulation of As in plant roots. Accumulation of As, instead, was found in transgenic tobacco plants where the *A. thaliana* ACR2 gene, coding for arsenate reductase, was expressed (Mandal, 2015).

Vacuole transporters can limit As transfer inside plants by mediating the transport of either free or phytochelatin-complexed arsenite into vacuoles. The *PvACR*3, coding for an As(III) antiporter in *P. vittata* (Indriolo et al., 2010), was expressed in *A. thaliana* and *N. tabacum*; both transgenic lines exhibited higher As retention in roots and lower accumulation in shoots than the respective WTs (Chen et al., 2017b). Hence, *PvACR3;*1 might be used to enhance As retention in roots and reduce its transfer to the above-ground biomass. In nature, higher plants do not possess ACR3-like transporters, but Song et al. (2010) identified a transporter for the transfer of As(III)-phytochelatin complexes in *A. thaliana* including an ATP Binding Cassette (ABC) transporter family member. In the same plant species, the identification of the carriers involved in the transport of As to phloem, silique, and seeds as inositol transporters

(INTs: INT2 and INT4) has enabled significant advance (Duan et al., 2016). These studies show that the extents of accumulated As can be affected in transgenic plants with either altered expression of a transporter gene or by heterologous expression. However, as suggested by Kumari et al. (2018), concerted changes in the expression of transporters involved in uptake, vacuolar sequestration, and translocation are needed to implement safe crops. Glutaredoxins (Grx) are proteins involved in As stress response of plants. Sundaram et al. (2009) expressed a *P. vittata* Grx gene (*i.e.*, *PvGRX5*) in *A. thaliana* and transgenic lines exhibited increased tolerance to As and lower accumulation in the above-ground biomass than the wild-type. The over-expression of two As-responsive Grx genes from rice (i.e., *OsGrx_C7* and *OsGrx_C2.1*) in *A. thaliana* led to similar results (Verma et al., 2016). *S*-adenosyl-methionine dependent methyltransferase is known to convert As(III) to the gaseous trimethylarsine (TMA) (Messens and Silver, 2006). *Chlamydomonas reinhardtii ArsM* was expressed in *A. thaliana* by Tang et al. (2016) who found that the vast majority of As was converted into dimethyl arsenate in transgenic plants along with other volatile forms. However, this modification led to a decreased tolerance to As, suggesting that although *ArsM* may increase its volatilization, this results in an altered As stress response in the plant.

The aim of some approaches was the improvement of the detoxification processes *via* increased synthesis of GSH and phytochelatins. In this respect, constitutive over-expression or heterologous expression of the critical enzymes involved in GSH and PCs biosynthesis, including γ-glutamylcysteine synthetase (γ-ECS), glutathione synthetase (GS) (Reisinger et al., 2008) and phytochelatin synthase (PCS) (Li et al., 2004; Picault et al., 2006; Gasic and Korban, 2007), moderately improved As tolerance and, in some instances, As accumulation decreased. Transgenic *A. thaliana* plants co-expressing *Allium sativum AsPCS1* and *γ-ECS* from *Saccharomyces cerevisiae* exhibited higher tolerance to As than WT plants (Guo et al., 2008). Transgenic lines of *A. thaliana*, over-expressing concomitantly PCS and γ-ECS, performed better than lines over-expressing one of the two genes in terms of increased As tolerance and reduced accumulation (Guo et al., 2008). Similar results were obtained by Wojas et al. (2010) with transgenic tobacco lines co-expressing *A. thaliana AtPCS1* and *CePCS* from *Caenorhabditis elegans*.

5. Conclusions

Edible crops play a relevant role in the entrance of arsenic in the food chain. A variety of plant-based approaches and agronomic practices to counteract the accumulation of arsenic in plants are currently available. An ever-increasing body of evidence suggests that

Table 3
Modified lines with altered tolerance to and accumulation capacity of arsenic in plant species, obtained either *via* expression of foreign genes into plant hosts other than rice or over-expression of wild-type genes.

Gene(s)	Product(s)	Gene source	Host	Main outcomes	Ref.
OsNRAMP1	Natural Resistance-Macrophage protein Transporter	*O. sativa*	*A. thaliana*	Roots and shoots of the transgenic line exhibited a two-fold higher concentration of As than the wild type (WT)	[1]
PvTIP4;1	Tonoplast intrinsic protein (TIP) transporter	*P. vittata*	*A. thaliana*	Significant increase in As accumulation in transgenic lines associated with enhanced susceptibility to As stress as compared to the WT	[2]
PvACR3;1	Arsenic compound resistance 3 (arsenite antiporter)	*P. vittata*	*A. thaliana* *N. tabaccum*	Higher As retention in roots and lower translocation to shoots in the transgenic line than the WTs	[3]
AtABCC1 *AtPCS1*	ATP binding cassette subfamily C transporter Phytochelatin synthase	*A. thaliana*	*A. thaliana*	Simultaneous over-expression of both genes led to in increased complexation of As by PCs enhanced transportation to the vacuole	[4]
AtPCS1	Phytochelatin synthase	*A. thaliana*	*B. juncea*	Significantly increased tolerance to As in transgenic line as compared to the WT	[5]
AtPCS1	Phytochelatin synthase	*A. thaliana*	*A. thaliana*	*A. thaliana* plants over-expressing AtPCS1from a strong constitutive *Arabidopsis* actin regulatory sequence (A2) exhibited marked resistant to arsenic	[6]
AtPCs1	Phytochelatin synthase	*A. thaliana*	*A. thaliana*	Plants that over-expressed *At*PCS1 in the cytoplasm exhibited higher tolerance to As than the WT. An opposite results was found when ATPCS1 was targeted to the chloroplast	[7]
ACR2	Arsenate reductase	*A. thaliana*	*N. tabaccum*	Higher tolerance to and lower accumulation of As in the transformant than the WT	[8]
GSH1 *AsPCS1*	γ-glutamylcysteine synthetase Phytochelatin synthase	*S. cerevisiae* *Allium sativum*	*A. thaliana*	Increased tolerance to As in both single- and double-gene transformants. Superiority of dual gene transformants over single ones	[9]
GSH1 *AsPCS1*	γ-glutamylcysteine synthetase Phytochelatin synthase	*E. coli* constructs	*B. juncea*	Enhanced tolerance to As in transgenics albeit with higher accumulation capacity than the WT	[10]
AtPCS1 *CePCS1*	Phytochelatin synthase	*A. thaliana* *C. elegans*	*N. tabacum*	Increased As-tolerance in the lines co-expressing both genes	[11]
PvGrx5	Glutaredoxin	*P. vittata*	*A. thaliana*	Improved tolerance to As in transgenic lines as a consequence of enhanced As(V) reduction and improved As (III) efflux *via* modulation of aquaglyceroporins	[12]
OsGrx_C7 *OsGrx_C2.1*	Glutaredoxin	*O. sativa*	*A. thaliana*	The transgenic expression of *OsGrx*s led to markedly reduced As accumulation in seeds and shoots associated with increased tolerance to As, as compared to the WT	[13]
CrarsM	SAM-methyltransferase	*C. reinhardtii*	*A. thaliana*	Acquisition by the transgenic line of a strong ability to methylate arsenic, associated, however, with increased susceptibility to As(III)	[14]

[1] Tiwari et al. (2014); [2] He et al. (2016); [3] Chen et al. (2017b); [4] Song et al. (2010); [5] Gasic and Korban (2007); [6] Li et al. (2004); [7] Picault et al. (2006); [8] Mandal (2015); [9] Guo et al. (2008); [10] Reisinger et al. (2008); [11] Wojas et al. (2010); [12] Sundaram et al. (2009); [13] Verma et al., 2016; [14] Tang et al. (2016).

genetic manipulation techniques can enhance the As-complexation ability of the plant and to increase the tolerance to arsenic in plants, and Table 3 summarizes these efforts. However, with the notable exception of rice (Chen et al., 2017a; Lindsay and Maathuis, 2017), these techniques have been applied to few crops, such as, for instance, Indian mustard (Gasic and Korban, 2007; Reisinger et al., 2008). To date, the majority of studies are confined to plant model systems such as *N. tabacum* and *A. thaliana* (Lindsay and Maathuis, 2017; Kumari et al., 2018). Apart from the limited application of genetic manipulation techniques to horticultural plants of relevant commercial interest, some considerations can be drawn. Several studies have had success in increasing the ability of the plant to complex arsenic through the manipulation of genes related to glutathione and phytochelatins. With a few exceptions (Song et al., 2010; Chen et al., 2017b), however, much work remains to be done to promote arsenic sequestration at the root level to prevent its transfer to the above-ground biomass. Even the practice of grafting, albeit consolidated and useful in increasing tolerance to heavy metals in horticultural plants, has remained confined only to a few cases for those elements, such as chromium and arsenic, which are present in the soil mainly in the form of oxyanions (Stazi et al., 2016; Balal et al., 2017). The known ability of the vast majority of higher plant species (around 90%) to interact with mycorrhizal species makes it likely and feasible the diffusion of this practice. Mycorrhizal fungi represent a significant component of the microbiota in the rhizosphere and can establish different associative forms with plants. Thus, extended use of the mycorrhization appears to be promising due to its reported ability to attenuate the As transfer from soil to plant (Smith et al., 2010; Garg et al., 2015; Spagnoletti et al.,2016, 2017).

Among agronomic practices, the use of inorganic amendments, mostly based on wastes containing iron and manganese oxides, turned out to be very effective in reducing the As uptake in a variety of horticultural plants. These successful results, unfortunately, have been often associated with marked reductions in biomass production. This drawback imposes the need for further investigations concerning the methods of application of these additives. As regards organic additives, given the controversial results observed concerning their ability to reduce the transfer of arsenic from the soil to the plant, it would be appropriate to focus attention on organic residues derived from thermochemical treatments carried out under strictly controlled conditions. The ever-growing knowledge of the characteristics of materials, such as biochar, as a function of the treatment conditions, can allow a targeted use and, above all, less dependent on the extreme variability of organic composted and non-composed materials (Uchimiya et al., 2013; Vithanage et al., 2017).

A planned and coordinated management of these options both on the local and wide-scale should require a mapping of the metal (loid)-contaminated areas aimed at providing a spatial database. Some efforts have been devoted to pursuing this goal, such as the FOREGS data produced by the EuroGeoSurvey and the continuous map sheet thereof derived (Lado et al., 2008) and the LUCAS Topsoil Survey (Tóth et al., 2016). A variety of remote and proximal sensing applications have been developed recently and shown to be able to provide reliable and robust estimates of total arsenic concentrations in soil (Choe et al., 2008; Shi et al., 2016; Pallottino et al., 2018). These applications, relying on visible and near-infrared reflectance spectroscopy associated with multivariate calibration, besides being rapid, cost-effective and suitable for the simultaneous estimation of metal (loid) concentrations in soil represent a valuable alternative to expensive and labor-consuming conventional methods.

Declarations of interest

None'

Acknowledgements

The research work has been supported by the Ministero dell'Istruzione, dell'Università e della Ricerca (Italy) (MIUR) [Grant number PRIN 2010JBNLJ7_006].

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