Nickel hyperaccumulation mechanisms: a review on the current state of knowledge

Teng-Hao-Bo Deng, Antony van der Ent, Ye-Tao Tang, Thibault Sterckeman, Guillaume Echevarria, Jean-Louis Morel, Rong-Liang Qiu

Public Monitoring Center for Agro-product of Guangdong, Academy of Agricultural Sciences, Guangzhou 510275, People's Republic of China

Centre for Mined Land Rehabilitation, Sustainable Minerals Institute, The University of Queensland, St Lucia, QLD 4072, Australia

Laboratoire Sols et Environnement, INRA-Université de Lorraine, 2 avenue de la Forêt de Haye, TSA 40602,
F-54518 Vandoeuvre-lès-Nancy Cédex, France

School of Environmental Science and Engineering, Sun Yat-sen University, Guangzhou 510275, People's Republic of China

Guangdong Provincial Key Laboratory of Environmental Pollution Control and Remediation Technology, Sun Yat-sen University, Guangzhou 510275, People's Republic of China

Abstract

Background Hyperaccumulator plants are unusual plants that accumulate particular metals or metalloids, such as nickel, zinc, cadmium and arsenic, in their living tissues to concentrations that are hundreds to thousands of times greater than what is normal for most plants. The hyperaccumulation phenomenon is rare (exhibited by less than 0.2% of all angiosperms), with most of the ~500 hyperaccumulator species known globally for nickel.

Scope This review highlights the contemporary under- standing of nickel hyperaccumulation processes, which include root uptake and sequestration, xylem loading and transport, leaf compartmentation and phloem trans-location processes.

Conclusions Hyperaccumulator plants have evolved highly efficient physiological mechanisms for taking up nickel in their roots followed by rapid translocation and sequestration into the aerial shoots. The uptake of nickel is mainly involved with low affinity transport systems, presumably from the ZIP family. The presence of high concentrations of histidine prevents nickel sequestration in roots. Nickel is efficiently loaded into the xylem, where it mainly presents as Ni^{2+}. The leaf is the main storage organ, which sequestrates nickel in non-active sites, e.g. vacuoles and apoplast. Recent studies show that phloem translocates high levels of nickel, which has a strong impact on nickel accumulation in young growing tissues.

Nickel hyperaccumulator plants: Discovery and application

Nickel (Ni) is the latest element to be considered essential for higher plants (Brown et al. 1987; Marschner 1995; Gerendas et al. 1999), due to its key role in urease, an enzyme that is widely distributed in higher plants (Hogan et al. 1983). The presence of urease prevents the accumulation of urea, which is generated during metabolic processes and is toxic to plants when presents in high concentrations. Apart from its function in urease activation, other physiological functions of Ni are poorly understood in higher plants (Gerendas et al. 1999). Although Ni is an essential micronutrient, its physiological requirement is extremely low. It is shown that 0.1 mg kg^{-1} or lower is sufficient for seed germination and plant growth (Brown et al. 1987; Gerendas et al. 1999). Hence, Ni deficiency in naturally-grown plants rarely occurs, and the only known case is for the pecan (Wood et al. 2004). Plants usually contain low concentrations of Ni, normally ranging from 0.01–5 mg kg^{-1} (Welch 1981). In contrast to the low Ni accumulation in normal plants, there is a group of plant species (hyperaccumulators) that can accumulate exceptional concentrations of Ni (>1000 mg kg^{-1} dry weight) in their living shoots without symptoms of toxicity (Brooks et al. 1977). Amazingly, up to 60.2 and 66.7 g kg^{-1} foliar Ni concentrations in the Ni hyperaccumulator *Phyllanthus* × *pallidus* from Cuba and *Alyssum cassium* from Turkey have been recorded (Reeves et al. 1996; Reeves and Adıgüzel 2008); while 25% Ni is found in the latex of the New Caledonian tree *Pycnandra acuminata*, and 16.9% Ni in the phloem sap exudates of the Malaysian tree *Phyllanthus balgooyi* (Jaffre et al. 1976; van der Ent and Mulligan 2015). At least 450 different Ni hyperaccumulating species have been discovered globally so far, most of which occur on tropical and subtropical ultramafic soils (Fig. 1) (van der Ent et al. 2013).

The extreme metal accumulation capability of hyperaccumulator plants spawned the concept of phytoextraction for remediating contaminated soils (Chaney 1983), which has attracted much research effort (Chaney et al. 1997; Salt et al. 1998; Pilon-Smits 2005; van der Ent et al. 2013). Hyperaccumulator plants also have potential for 'phytomining' which utilizes hyperaccumulators as 'metal crops' to sequester Ni in harvestable biomass that can then be used to produce fine Ni chemicals or ecocatalysts (Chaney 1983; Li et al. 2003; Zhang et al. 2014; van der Ent et al. 2015; Nkrumah et al. 2016). Phytomining of Ni is especially promising, due to the high market price of Ni, the large variety of hyperaccumulating species adapted to a wide climatic range, and numerous tracts of suitable application areas, e.g. natural ultramafic soils (van der Ent et al. 2015). Phytomining has been demonstrated at field scale in a few countries around the world (Nicks and Chambers 1995; Robinson et al. 1997a; Robinson et al. 1997b; Li et al. 2003; Bani et al. 2007; Bani et al. 2015).

The optimization of phytomining/phytoextraction technologies requires in-depth knowledge of the metal uptake and transport mechanisms in hyperaccumulator plants. For example, unravelling the pathways associated with Ni uptake will allow for a better application of specific soil amendments to increase the Ni extraction yield in metal crops. Furthermore, insight into the physiological mechanisms of metal hyperaccumulation has important implications for advancing the understanding of the uptake and transport of trace elements in 'normal plants' such as food crops (Bai et al. 2007; White and Broadley 2011).

Nickel hyperaccumulation mechanisms

Recent decades have witnessed much progress in our understanding of the physiology of hyperaccumulator plants, mainly focusing on Zn and Cd hyperaccumulation processes in Brassicaceae (Krämer 2010). The hyperaccumulation mechanisms generally include stimulated metal absorption in roots, reduced metal sequestration in root vacuoles, efficient xylem loading and xylem transport, strong metal sequestration and compartmentation in leaves (Milner and Kochian 2008; Verbruggen et al. 2009) (Fig. 2). Less is known regarding the physiology of Ni hyperaccumulator plants. The Ni hyperaccumulation mechanisms share

similarities with those of Zn, while also having distinct characteristics. Here we will review contemporary knowledge on root uptake, root sequestration, xylem loading, leaf compartmentation and phloem translocation processes of Ni hyperaccumulator plants.

Nickel uptake processes

Indirect evidence has suggested that hyperaccumulator plants absorb Ni mainly as Ni^{2+}, which is the same as non-hyperaccumulators. For example, the addition of chelating agents (citric acid, EDTA, NTA, DTPA, etc.) reduces the uptake of Ni by *Berkheya coddii* in spite of an increase in the available Ni content in soils (Robinson et al. 1997a; Robinson et al. 1999), which is presumably due to a reduction of the Ni^{2+} concentration in the soil solution. Likewise, halving the Ni^{2+} activity in hydroponic culture solutions results in a 50% reduction of the Ni uptake rate in the roots of *Noccaea goesingense* (Puschenreiter et al. 2005).

Few studies have been conducted to investigate the Ni^{2+} uptake kinetics. For non-hyperaccumulators, Ni absorption in roots has been found to be metabolic- dependent, which can be inhibited by low temperature, metabolic inhibitors and anaerobic conditions (Aschmann and Zasoski 1987). Nickel uptake has been suggested to be a kinetic process, which fits the Michaelis-Menten kinetics, with Michaelis-Menten constant values (Km) ranging from 0.51–379 μM (Cataldo et al. 1978; Aschmann and Zasoski 1987; Zhang et al. 2001; Redjala et al. 2010). The relatively high Km values indicate that Ni^{2+} is mainly absorbed via low-affinity transport systems in the plants (soybean, oat plant, mung bean, maize, etc.). The interaction between Ni^{2+} and other divalent cations has been observed during the root uptake process. For example, competition kinetic studies show that Cu^{2+} and Zn^{2+} competitively inhibited Ni^{2+} influx, while Ca^{2+} and Mg^{2+} were non-competitive inhibitors of Ni^{2+} in soybean and barley (Cataldo et al. 1978; Körner et al. 1987). In *Arabidopsis thaliana*, Fe deficiency results in Ni accumulation in roots (Nishida et al. 2011). Molecular studies show that Ni^{2+} can be absorbed via the ferrous transporter IRT1 in *A. thaliana* (Nishida et al. 2011; Nishida et al. 2012), due to the lack of substrate specificity of AtIRT1 (Schaaf et al. 2006). These results suggest that in non-hyperaccumulators, Ni may be mainly absorbed via the low-affinity transport systems of other divalent micro-nutrient elements, e.g. Zn, Fe and Cu. A similar Ni^{2+} uptake pattern seems to exist in Ni hyperaccumulator plants. For the Zn/Ni hyperaccumulator *Noccaea pindica*, Ni uptake is inhibited by the addition of Zn^{2+} in hydroponic culture solution, whereas Ni has little effect on Zn uptake (Taylor and Macnair 2006). Likewise, even the Ni- hyperaccumulating populations of *N. caerulescens* still preferred Zn over Ni (Assunção et al. 2001). These results suggest that the Zn/Ni hyperaccumulating Noccaea species possess both Zn-specific high-affinity uptake systems, functioning on Zn^{2+} absorption which cannot be affected by Ni^{2+}, and low-affinity Zn/Ni up- take systems, which functions on both Zn^{2+} and Ni^{2+} absorption. Isotope fractionation study has shown that the Zn/Ni hyperaccumulator *N. caerulescens* and the Ni hyperaccumulator *Alyssum murale* share similar Ni isotope fractionation patterns, which enriched light Ni isotopes; while Zn can compete with Ni during the uptake process, which severely reduces Ni concentrations in plants and decreases the extent of Ni isotope fractionation (Deng et al. 2014). This suggests that although *A. murale* is not a Zn hyperaccumulator, it may also take up Ni^{2+} via the low-affinity transport systems of Zn2+. Ni uptake also seems to involve Fe transporter(s). For example, in the Ni hyperaccumulator *Alyssum inflatum*, Fe accumulation in roots was stimulated by elevated Ni concentrations (Ghasemi et al. 2009). Far less is known on the molecular basis of Ni^{2+} uptake processes. SOLiD high-throughput sequencing of the root transcriptomes in N. caerulescens has shown that Ni exposure can stimulate the gene expression of both the Fe^{2+} transporter IRT1 and the Zn transporter ZIP10, which suggests that Ni uptake may be involved with low-affinity transporters from the ZIP family (Halimaa et al. 2014). To the best of our knowledge, no high-affinity Ni influx transporter(s) have been identified in hyperaccumulators, or in other higher plants.

Root sequestration processes

On reaching root symplast, metal ions are rapidly complexed by organic ligands to alleviate toxicity (Haydon and Cobbett 2007). Amino acids are favourable for metal complexation under the alkaline conditions of cytoplasmic matrix (Harris et al. 2012). Histidine concentrations are found to be constitutively high in roots of the Ni hyperaccumulator *Alyssum lesbiacum* in comparison to the non-hyperaccumulator *Brassica juncea* (Kerkeb and Krämer 2003), which results from the overexpression of the histidine biosynthetic pathway in this species (Ingle et al. 2005). Interestingly, Ni^{2+} chelation with histidine can suppress Ni sequestration into root vacuoles, and thus enhance Ni mobility and facilitate its radial transport in root symplast, which is quite similar to that of Zn (Richau et al. 2009; Kozhevnikova et al. 2014b). Supplying histidine to hyperaccumulators can increase Ni tolerance and root- shoot transport simultaneously (Krämer et al. 1996; Kerkeb and Krämer 2003). Therefore, histidine acts as a Ni transport facilitator in the cytoplasmic matrix of root cells. However, carboxylic acids may still be the main chelators for Ni in roots, in particular when relatively high concentration of Ni is sequestrated into root vacuoles after long cultivation periods (Montargès-Pelletier et al. 2008).

Xylem loading and transport processes

On reaching xylem parenchyma, Ni is loaded from root symplast to xylem vessels. Both hyperaccumulator and non-hyperaccumulators may possess similar efflux transporter(s) during the xylem loading processes, as the root to shoot Ni translocation rates are the same in both species (Krämer et al. 1997b). Antagonistic effects between Ni and Zn were found during the root-shoot transport of the Ni hyperaccumulating populations of *N. caerulescens* (Assunção et al. 2001). In addition, Ni can inhibit root-shoot translocation of Fe in the Ni hyperaccumulator *A. inflatum* (Ghasemi et al. 2009). These results indicate that Ni may be partly loaded by Zn/Fe efflux transport systems. However, no specific Ni efflux transporter has as yet been identified. When entering xylem vessels, Ni transport is mainly driven by leaf transpiration (Robinson et al. 2003; Centofanti et al. 2012). The Ni speciation in xylem sap has been studied in a number of hyperaccumulator plants. In A. lesbiacum, 48% Ni in xylem sap remains in the form of free hydrated cation, while other Ni is chelated by histidine (19%), glutamine (15%), citrate (9%) and malate (3%) (Krämer et al. 1996). Nicotianamine-bound Ni comprises a small fraction (8.5%) of the total Ni in xylem sap of *N. caerulescens* (Mari et al. 2006). A field investigation has shown that Ni in the xylem sap of *Alyssum serpyllifolium* subsp. *lusitanicum* mainly exists as free hydrated cation (about 70%), or complexes with carboxylic acids, e.g. citric acid (18%) (Alves et al. 2011). It is demonstrated that the concentrations of organic ligands are too low to account for complete Ni chelation in xylem sap, suggesting that most of the Ni in xylem sap remains as hydrated cation (Centofanti et al. 2013). This is a reasonable finding as Ni^{2+} is quite stable in acidic xylem sap (pH 5–6), and xylem vessels are non-living cells which should not be affected by high concentrations of Ni^{2+}.

Xylem unloading and leaf compartmentation processes

On reaching leaves, the main storage organ, Ni is then transferred across the whole apoplastic space via leaf veins. Here, Ni is either absorbed by leaf cells (symplast), or remains in the apoplast. Firstly, Ni absorption by leaf cells may involve trans- porters from the ZIP family, e.g. ZNT1 and ZNT2, as the gene expression of these transporters can be up regulated by Ni exposure (Visioli et al. 2014). Nickel is preferentially distributed in epidermal cells, the least active tissue of leaf symplast (Küpper et al. 2001; Tappero et al. 2007), while palisade mesophyll cells become an increasingly important compartment as Ni concentrations in leaves increase (Broadhurst et al. 2004). At the subcellular level, Ni is mainly accumulated in leaf vacuoles (Krämer et al. 2000; Robinson et al. 2003). Molecular studies have shown that cation efflux transporters, e.g. MTP1 (in *N. goesingense*) or IREG1 (in *Psychotria gabriellae*), are highly expressed in the tonoplast of leaf cells (Persans et al. 2001; Merlot et al. 2014); while Ni^{2+}/n^{H+} antiport activity driven by V-ATPase, is also found at

the tonoplast of *A. lesbiacum* (Ingle et al. 2008), whose function is to transport Ni into leaf vacuoles. Ni in leaf cells is generally complexed by carboxylic acids. For example, citric acid is the main ligand for Ni in several woody hyperaccumulators from New Caledonia (Lee et al. 1977, 1978; Callahan et al. 2012). While in the herbaceous *Alyssum* species, Ni is principally associated with malic and malonic acids (Brooks et al. 1981; Montargès-Pelletier et al. 2008). Secondly, leaf apoplast also acts as an important sink for redundant Ni, in particular when large amounts of Ni^{2+} are transported to leaves from the xylem. For example, cell walls, cuticles, epidermal trichomes can store high concentrations of Ni (Krämer et al. 1997a; Krämer et al. 2000; Robinson et al. 2003). In addition, Ni enrichment is also observed in leaf tips, probably resulting from the release of excess Ni with guttation fluids (McNear et al. 2005).

Phloem translocation processes

From the studies on non-hyperaccumulators, Ni is known to be relatively mobile in phloem and can be readily transferred from sources (generally mature leaves) to sinks (young growing tissues) (Neumann and Chamel 1986; Page and Feller 2005; Page et al. 2006). Phloem translocation is bidirectional, which includes both downward and upward movements. Results showed that radioactive ^{63}Ni fed into the leaf lamina of wheat, lettuce, radish and bean, can be rapidly transferred up to younger leaves and seeds, and down to roots (Fismes et al. 2005; Riesen and Feller 2005). The only study regarding Ni speciation in phloem sap found that in *Ricinus communis*, Ni is mainly bound to organic compounds with a molecular weight in the range of 1000–5000 (Wiersma and van Goor 1979). The phloem translocation process i n hyperaccumulator plants has long been ignored, since heavy metals are considered to be 'firmly' sequestrated in leaves. However, field surveys have already shown that seeds and flowers of hyperaccumulator plants can accumulate Ni as high as that in leaves (Zhang et al. 2014; Groeber et al. 2015). As reproductive organs are the main sink of phloem translocation, this circumstantial evidence indicates that hyperaccumulator plants can translocate substantial amount of Ni via phloem. As a matter of fact, Ni enrichment in phloem has been documented in a number of woody hyperaccumulators growing on tropical ultramafic soils. For example, 3.1% Ni is found in the phloem sap of *Euphorbia helenae* subsp. *grandifolia* from Cuba (Reeves et al. 1996). Recent field investigation reveals that *Phyllanthus balgooyi* from Sabah, Malaysia, has an exceptionally Ni-rich phloem sap exudates that contains up to 16.9% Ni (van der Ent and Mulligan 2015; Mesjasz-Przybylowicz et al. 2016). In the herbaceous hyperaccumulator N. caerulescens, both Ni and Zn are found to be enriched in leaf phloem exudates of the Zn/Ni hyperaccumulator (Deng et al. 2016). Taken together, these results indicate that hyperaccumulator plants have strong Ni phloem loading capabilities.

Ni speciation in phloem is quite different from that in xylem. For example, in *P. balgooyi*, Ni in phloem is mainly complexed by citrate (van der Ent et al. 2017). While in N. caerulescens, malate is the dominant organic acids and is considered to be the main chelator for phloem Ni (Deng et al. 2016). Therefore, it seems that Ni translocation in phloem is facilitated by carboxylic acids. For bidirectional translocation in phloem, Deng et al. (2016) found that 89% of the Ni exported from old leaves of N. caerulescens is translocated upward to young leaves, whereas only 11% moves downward to roots. This result suggests that upward movement is the dominant direction for phloem translocation, and that young leaves and reproductive organs are the main sink for phloem-based Ni. Also, Estrade et al. (2015) found that Ni isotope fractionation between leaves and flowers does occur in early growing stages of *A. murale* as a result of net Ni transfer to leaves. While at full flowering stage, Ni isotope compositions between leaves and flowers are leveled up, which indicates that intense phloem redistribution occurs at this stage. Given that phloem sap contains high concentration of Ni, phloem translocation can have great impact on the Ni accumulation of the young growing tissues (young leaves, flowers, seeds, etc.) of hyperaccumulator plants. A conceptual model for Ni hyperaccumulation mechanisms is proposed in Fig. 3, and consists of nine physiological processes, as follows:

Rhizospheric Ni^{2+} is efficiently absorbed into root symplast via low-affinity transport systems, which mainly belong to Zn and Fe transporters. In root cytoplasm, assimilated Ni ions are readily chelated by organic compounds, e.g. histidine. Due to the weak sequestration capacity of root vacuoles, most Ni will then be transferred radially from epidermis to pericycle.

Nickel is then efficiently exported from xylem parenchyma and loaded into xylem vessels, which may be due to the high expression of Ni efflux transporter(s) at parenchyma cell membranes.

Nickel moves up to shoots following the xylem flow, most of which find their final destination in mature leaves due to the strong transpiration in these tissues, while young leaves receive relatively small proportion of Ni in xylem. Nickel is present mainly in the form of free hydrated cations during xylem transport. As xylem flow reaches minor veins and fills in the apoplastic space in leaves, Ni is then unloaded into the leaf symplast, or remains in apoplast.

Nickel assimilated by leaf symplast is readily transferred into vacuoles, in particular in epidermis cells. Nickel in vacuoles is mainly chelated by carboxylic acids. Phloem companion cells, which are soaked in Ni- rich apoplastic fluid, may express highly-efficient Ni influx transporters, which absorb large quantities of Ni^{2+} into the cytosols. The assimilated Ni^{2+} is chelated by a variety of carboxylic acids, e.g. malate or citrate.

Nickel-ligand complexes are then transferred from companion cells to phloem sieve elements via plasmodesmata. Nickel moves passively in sieve elements, following the phloem flow, which is mainly driven by osmotic pressure generated by photosynthate (mainly sucrose) concentration gradients between sources and sinks. Upward movement appears to be the main direction for phloem translocation. When reaching sink organs (young growing tis- sues), Ni may be exported out from phloem tissues to the apoplast again, which is then taken up by the surrounding cells.

Knowledge gaps and scope for future research

On the basis of the current state of knowledge, a picture emerges of the Ni uptake and transport in hyperaccumulator plants. However, more details are waiting to be explored, in particular on the molecular and genetic level. Open questions include:

What Ni transporter(s) are involved during the root uptake processes?

Nickel is found to be absorbed mainly via low- affinity transporters of Zn and Fe in the Ni hyperaccumulating and Zn-non-accumulating plant species. Do distinct Ni influx transporters exist in these species and how is the expression of the genes regulated?

How can Ni be efficiently loaded into xylem?

Hyperaccumulator plants must possess efficient Ni efflux transporters in xylem parenchyma. However, little is known about these transporters and whether they are Ni-specific or can bind to a range of divalent cations.

How is Ni loaded and unloaded into phloem?

Phloem translocation in hyperaccumulator plants has yet to be studied in depth. In order to identify the Ni phloem loading and unloading process, the connection between phloem tissue and phloem parenchyma (e.g. mesophyll cells) must be clarified. For some species, such as *A. thaliana*, the phloem tissues are separated from surrounding cells due to the lack of plasmodesmata connections (Haritatos et al. 2000), and thus metals are loaded into and unloaded from phloem via apoplast. In some other species, there are numerous

plasmodesmata at the interface between phloem tissues and surrounding cells (Taiz and Zeiger 2010), which can transfer metals from mesophyll into sieve element–companion cell complex symplastically, and vice versa. However, the phloem structure of Ni hyperaccumulator plants is largely unknown. If apoplastic loading/unloading of Ni is the dominant process, then the identification of Ni transmembrane transporters on sieve element and companion cells is of particular interest.

To what extent does phloem translocation of Ni play a role in Ni hyperaccumulation?

Phloem translocation is a bidirectional movement which transfers phloem fluids up to growing tissues (young leaves, flowers, seeds, etc.), and down to roots. If large quantities of Ni are transported back to roots and/or soils, that would have great significance for the Ni uptake in hyperaccumulator plants. Thus, it is relevant to quantify the fluxes of Ni from phloem sources to sinks.

What are the physiological differences within hyperaccumulator species?

Nickel hyperaccumulator plants are widely distributed, both geographically and across phylogenies, suggesting that physiological processes of hyperaccumulation have evolved independently and may therefore differ in their function between species. For example, citrate is the main chelator for Ni in leaves and phloem of tropical woody Ni hyperaccumulator plants, while this is malate for herbaceous species. Moreover, green-colored phloem sap which is highly Ni-enriched has been found in a number of tropical species, such as P. balgooyi, but as yet not in other herbaceous Ni hyperaccumulators, e.g. *A. murale* or *N. caerulescens*, or any other higher plants. Thus, the differences within Ni hyperaccumulator species warrant further investigation.

Acknowledgements

We thank Dr. Wang Shi-Zhong and Helen Selliez for their constructive comments on this study. This work was supported by the National Natural Science Foundation of China (No. 41701369, No.41371315, No.41401367), Natural Science Foundation of Guangdong Province, China (No. 2014A030313570, 2017A030310505), Science and Technology Project of Guangdong Province, China (No. 2014A020208067) and Presidential Foundation of Guangdong Academy of Agricultural Science (201801). The French National Research Agency through the national Investissements d'avenir program (ANR-10-LABX-21, LABEX RESSOURCES21) and through the ANR-14-CE04-0005 Project Agromine is acknowledged for funding support. A. van der Ent is the recipient of a Discovery Early Career Researcher Award (DE160100429) from the Australian Research Council.

References

Alves S, Nabais C, Simões Gonçalves ML, Correia dos Santos MM (2011) Nickel speciation in the xylem sap of the hyperaccumulator *Alyssum serpyllifolium* Ssp. *lusitanicum* growing on serpentine soils of northeast Portugal. J Plant Physiol 168:1715–1722

Aschmann S, Zasoski R (1987) Nickel and rubidium uptake by whole oat plants in solution culture. Physiol Plant 71:191– 196

Assunção AGL, Martins PDC, De Folter S, Vooijs R, Schat H, Aarts MGM (2001) Elevated expression of metal transporter genes in three accessions of the metal hyperaccumulator *Thlaspi caerulescens*. Plant Cell Environ 24:217–226

Bai C, Reilly CC, Wood BW (2007) Nickel deficiency affects nitrogenous forms and urease activity in spring xylem sap of pecan. J Am Soc Hortic Sci 132:302–309

Bani A, Echevarria G, Sulçe S, Morel J, Mullai A (2007) In-situ phytoextraction of Ni by a native population of *Alyssum murale* on an ultramafic site (Albania). Plant Soil 293:79–89

Bani A, Echevarria G, Sulçe S, Morel JL (2015) Improving the agronomy of *Alyssum Murale* for extensive phytomining: a five-year field study. Int J Phytoremediat 17:117–127

Broadhurst CL, Chaney RL, Angle JS, Erbe EF, Maugel TK (2004) Nickel localization and response to increasing Ni soil levels in leaves of the Ni hyperaccumulator *Alyssum murale*. Plant Soil 265:225–242

Brooks RR, Lee J, Reeves RD, Jaffre T (1977) Detection of nickeliferous rocks by analysis of herbarium specimens of indicator plants. J Geochem Explor 7:49–57

Brooks RR, Shaw S, Asensi Marfil A (1981) The chemical form and physiological function of nickel in some Iberian *Alyssum* species. Physiol Plant 51:167–170

Brown PH, Welch RM, Cary EE (1987) Nickel: a micronutrient essential for higher plants. Plant Physiol 85:801–803

Callahan DL, Roessner U, Dumontet V, De Livera AM, Doronila A, Baker AJM, Kolev SD (2012) Elemental and metabolite profiling of nickel hyperaccumulators from New Caledonia. Phytochemistry 81:80–89

Cataldo DA, Garland TR, Wildung RE (1978) Nickel in plants: I. Uptake kinetics using intact soybean seedlings. Plant Physiol 62:563–565

Centofanti T, Siebecker M, Chaney R, Davis A, Sparks D (2012) Hyperaccumulation of nickel by *Alyssum corsicum* is related to solubility of Ni mineral species. Plant Soil 359:71–83

Centofanti T, Sayers Z, Cabello-Conejo M, Kidd P, Nishizawa N, Kakei Y, Davis A, Sicher R, Chaney R (2013) Xylem exudate composition and root-to-shoot nickel translocation in *Alyssum* species. Plant Soil 373:59–75

Chaney RL (1983) Plant uptake of inorganic waste constituents. Land Treat Hazard Wastes 5:50–76

Chaney RL, Malik M, Li YM, Brown SL, Brewer EP, Angle JS, Baker AJM (1997) Phytoremediation of soil metals. Curr Opin Biotech 8:279–284

Deng T-H-B, Cloquet C, Tang Y-T, Sterckeman T, Echevarria G, Estrade N, Morel J-L, Qiu R-L (2014) Nickel and zinc isotope fractionation in hyperaccumulating and nonaccumulating plants. Environ Sci Technol 48:11926– 11933

Deng T-H-B, Tang Y-T, van der Ent A, Sterckeman T, Echevarria G, Morel J-L, Qiu R-L (2016) Nickel translocation via the phloem in the hyperaccumulator *Noccaea caerulescens* (Brassicaceae). Plant Soil 404:35–45

Estrade N, Cloquet C, Echevarria G, Sterckeman T, Deng T, Tang Y, Morel J-L (2015) Weathering and vegetation controls on nickel isotope fractionation in surface ultramafic environments (Albania). Earth Planet Sc Lett 423:24–35

Fismes J, Echevarria G, Leclerc-Cessac E, Morel JL (2005) Uptake and transport of radioactive nickel and cadmium into three vegetables after wet aerial contamination. J Environ Qual 34:1497–1507

Gerendas J, Polacco JC, Freyermuth SK, Sattelmacher B (1999) Significance of nickel for plant growth and metabolism. J Plant Nutr Soil Sc 162:241–256

Ghasemi R, Ghaderian SM, Krämer U (2009) Interference of nickel with copper and iron homeostasis contributes to metal toxicity symptoms in the nickel hyperaccumulator plant *Alyssum inflatum*. New Phytol 184:566–580

Groeber S, Przybyłowicz W, Echevarria G, Montarges-Pelletier E, Barnabas A, Mesjasz-Przybyłowicz J (2015) Fate of nickel and calcium in seedlings of the hyperaccumulator *Berkheya coddii* during germination. Biol Plantarum 59:560–569

Halimaa P, Lin Y-F, Ahonen VH, Blande D, Clemens S, Gyenesei A, Häikiö E, Kärenlampi SO, Laiho A, Aarts MGM, Pursiheimo J-P, Schat H, Schmidt H, Tuomainen MH, Tervahauta AI (2014) Gene expression differences between *Noccaea caerulescens* ecotypes help to identify candidate genes for metal phytoremediation. Environ Sci Technol 48: 3344–3353

Haritatos E, Medville R, Turgeon R (2000) Minor vein structure and sugar transport in *Arabidopsis thaliana*. Planta 211:105– 111

Harris WR, Sammons RD, Grabiak RC (2012) A speciation model of essential trace metal ions in phloem. J Inorg Biochem 116: 140–150

Haydon MJ, Cobbett CS (2007) Transporters of ligands for essential metal ions in plants. New Phytol 174:499–506

Hogan ME, Swift IE, Done J (1983) Urease assay and ammonia release from leaf tissues. Phytochemistry 22:663–667

Ingle RA, Mugford ST, Rees JD, Campbell MM, Smith JAC (2005) Constitutively high expression of the histidine biosynthetic pathway contributes to nickel tolerance in hyperaccumulator plants. Plant Cell 17:2089–2106

Ingle RA, Fricker MD, Smith JAC (2008) Evidence for nickel/ proton antiport activity at the tonoplast of the hyperaccumulator plant *Alyssum lesbiacum*. Plant Biol 10: 746–753

Jaffre T, Brooks RR, Lee J, Reeves RD (1976) *Sebertia acuminata*: a hyperaccumulator of nickel from New Caledonia. Science 193:579–580

Kerkeb L, Krämer U (2003) The role of free histidine in xylem loading of nickel in *Alyssum lesbiacum* and *Brassica juncea*. Plant Physiol 131:716–724

Körner LE, Møller LM, Jensén P (1987) Effects of Ca2+ and other divalent cations on uptake of Ni2+ by excised barley roots. Physiol Plant 71:49–54

Kozhevnikova AD, Seregin IV, Verweij R, Schat H (2014) Histidine promotes the loading of nickel and zinc, but not of cadmium, into the xylem in *Noccaea caerulescens*. Plant Signal Behav 9:e29580

Krämer U (2010) Metal hyperaccumulation in plants. Annu Rev Plant Biol 61:517–534

Krämer U, Cotter-Howells JD, Charnock JM, Baker AJM, Smith JAC (1996) Free histidine as a metal chelator in plants that accumulate nickel. Nature 379:635–638

Krämer U, Grime GW, Smith JAC, Hawes CR, Baker AJM (1997a) Micro-PIXE as a technique for studying nickel lo-calization in leaves of the hyperaccumulator plant *Alyssum lesbiacum*. Nucl Instrum Methods Phys Res, Sect B 130: 346–350

Krämer U, Smith RD, Wenzel WW, Raskin I, Salt DE (1997b) The role of metal transport and tolerance in nickel hyperaccumulation by *Thlaspi goesingense* Halacsy. Plant Physiol 115:1641–1650

Krämer U, Pickering IJ, Prince RC, Raskin I, Salt DE (2000) Subcellular localization and speciation of nickel in hyperaccumulator and non-accumulator *Thlaspi* species. Plant Physiol 122:1343–1353

Küpper H, Lombi E, Zhao FJ, Wieshammer G, McGrath SP (2001) Cellular compartmentation of nickel in the hyperaccumulators *Alyssum lesbiacum, Alyssum bertolonii* and *Thlaspi goesingense*. J Exp Bot 52:2291–2300

Lee J, Reeves RD, Brooks RR, Jaffré T (1977) Isolation and identification of a citrato-complex of nickel from nickel- accumulating plants. Phytochemistry 16:1503–1505

Lee J, Reeves RD, Brooks RR, Jaffré T (1978) The relation between nickel and citric acid in some nickel-accumulating plants. Phytochemistry 17:1033–1035

Li Y-M, Chaney R, Brewer E, Roseberg R, Angle JS, Baker A, Reeves R, Nelkin J (2003) Development of a technology for commercial phytoextraction of nickel: economic and technical considerations. Plant Soil 249:107–115

Mari S, Gendre D, Pianelli K, Ouerdane L, Lobinski R, Briat JF, Lebrun M, Czernic P (2006) Root-to-shoot long-distance circulation of nicotianamine and nicotianamine-nickel chelates in the metal hyperaccumulator *Thlaspi caerulescens*. J Exp Bot 57:4111–4122

Marschner H (1995) Mineral nutrition of higher plants, 2nd edn. Academic, London

McNear DH, Peltier E, Everhart J, Chaney RL, Sutton S, Newville M, Rivers M, Sparks DL (2005) Application of quantitative fluorescence and absorption-edge computed microtomography to image metal compartmentalization in *Alyssum murale*. Environ Sci Technol 39:2210–2218

Merlot S, Hannibal L, Martins S, Martinelli L, Amir H, Lebrun M, Thomine S (2014) The metal transporter PgIREG1 from the hyperaccumulator *Psychotria gabriellae* is a candidate gene for nickel tolerance and accumulation. J Exp Bot 65:1551– 1564

Mesjasz-Przybylowicz J, Przybylowicz W, Barnabas A, van der Ent A (2016) Extreme nickel hyperaccumulation in the vascular tracts of the tree *Phyllanthus balgooyi* from Borneo. New Phytol 209:1513–1526

Milner MJ, Kochian LV (2008) Investigating heavy-metal hyperaccumulation using *Thlaspi caerulescens* as a model system. Ann Bot-London 102:3–13

Montargès-Pelletier E, Chardot V, Echevarria G, Michot LJ, Bauer A, Morel J-L (2008) Identification of nickel chelators in three hyperaccumulating plants: an X-ray spectroscopic study. Phytochemistry 69:1695–1709

Neumann PM, Chamel A (1986) Comparative phloem mobility of nickel in nonsenescent plants. Plant Physiol:689–691

Nicks L, Chambers M (1995) Farming for metals. Mining. Environ Manag 3:15–16

Nishida S, Tsuzuki C, Kato A, Aisu A, Yoshida J, Mizuno T (2011) AtIRT1, the primary iron uptake transporter in the root, mediates excess nickel accumulation in *Arabidopsis thaliana*. Plant Cell Physiol 52:1433–1442

Nishida S, Aisu A, Mizuno T (2012) Induction of IRT1 by the nickel-induced iron-deficient response in *Arabidopsis*. Plant Signal Behav 7:329–331

Nkrumah PN, Baker AJM, Chaney RL, Erskine PD, Echevarria G, Morel JL, van der Ent A (2016) Current status and challenges in developing nickel phytomining: an agronomic perspective. Plant Soil 406:55–69

Page V, Feller U (2005) Selective transport of zinc, manganese, nickel, cobalt and cadmium in the root system and transfer to the leaves in young wheat plants. Ann Bot-London 96:425– 434

Page V, Weisskopf L, Feller U (2006) Heavy metals in white lupin: uptake, root-to-shoot transfer and redistribution within the plant. New Phytol 171:329–341

Persans MW, Nieman K, Salt DE (2001) Functional activity and role of cation- efflux family members in Ni hyperaccumulation in *Thlaspi goesingense*. Proc Natl Acad Sci 98:9995–10000

Pilon-Smits E (2005) Phytoremediation. Annu Rev Plant Biol 56: 15–39

Puschenreiter M, Schnepf A, Millán IM, Fitz WJ, Horak O, Klepp J, Schrefl T, Lombi E, Wenzel WW (2005) Changes of Ni biogeochemistry in the rhizosphere of the hyperaccumulator *Thlaspi goesingense*. Plant Soil 271:205–218

Redjala T, Sterckeman T, Skiker S, Echevarria G (2010) Contribution of apoplast and symplast to short term nickel uptake by maize and *Leptoplax emarginata* roots. Environ Exp Bot 68:99–106

Reeves RD, Adigüzel N (2008) The nickel hyperaccumulating plants of the serpentines of Turkey and adjacent areas: a review with new data. Turk J Biol 32:143–153

Reeves RD, Baker AJM, Borhidi A, Berazain R (1996) Nickel-accumulating plants from the ancient serpentine soils of Cuba. New Phytol 133:217–224

Richau KH, Kozhevnikova AD, Seregin IV, Vooijs R, Koevoets PLM, Smith JAC, Ivanov VB, Schat H (2009) Chelation by histidine inhibits the vacuolar sequestration of nickel in roots of the hyperaccumulator *Thlaspi caerulescens*. New Phytol 183:106–116

Riesen O, Feller U (2005) Redistribution of nickel, cobalt, man- ganese, zinc, and cadmium via the phloem in young and maturing wheat. J Plant Nutr 28:421–430

Robinson BH, Brooks RR, Howes AW, Kirkman JH, Gregg PEH (1997a) The potential of the high-biomass nickel hyperaccumulator *Berkheya coddii* for phytoremediation and phytomining. J Geochem Explor 60:115–126

Robinson BH, Chiarucci A, Brooks RR, Petit D, Kirkman JH, Gregg PEH, De Dominicis V (1997b) The nickel hyperaccumulator plant Alyssum bertolonii as a potential agent for phytoremediation and phytomining of nickel. J Geochem Explor 59:75–86

Robinson BH, Brooks RR, Clothier BE (1999) Soil amendments affecting nickel and cobalt uptake by *Berkheya coddii*: potential use for phytomining and phytoremediation. Ann Bot-London 84:689–694

Robinson BH, Lombi E, Zhao FJ, McGrath SP (2003) Uptake and distribution of nickel and other metals in the hyperaccumulator Berkheya coddii. New Phytol 158:279– 285

Salt DE, Smith R, Raskin I (1998) Phytoremediation. Annu Rev Plant Biol 49:643–668

Schaaf G, Honsbein A, Meda AR, Kirchner S, Wipf D, von Wirén N (2006) AtIREG2 encodes a tonoplast transport protein involved in iron-dependent nickel detoxification in *Arabidopsis thaliana* roots. J Biol Chem 281:25532–25540

Taiz L, Zeiger E (2010) Plant Physiol, 5th edn. Sinauer Associates, Sunderland

Tappero R, Peltier E, Gräfe M, Heidel K, Ginder-Vogel M, Livi KJT, Rivers ML, Marcus MA, Chaney RL, Sparks DL (2007) Hyperaccumulator *Alyssum murale* relies on a different metal storage mechanism for cobalt than for nickel. New Phytol 175:641–654

Taylor SI, Macnair MR (2006) Within and between population variation for zinc and nickel accumulation in two species of *Thlaspi* (Brassicaceae). New Phytol 169:505–514

van der Ent A, Mulligan D (2015) Multi-element concentrations in plant parts and fluids of Malaysian nickel hyperaccumulator plants and some economic and ecological considerations. J Chem Ecol 41:396–408

van der Ent A, Baker AM, Reeves R, Pollard AJ, Schat H (2013) Hyperaccumulators of metal and metalloid trace elements: facts and fiction. Plant Soil 362:319–334

van der Ent A, Baker A, Reeves R, Chaney R, Anderson CWN, Meech J, Erskine P, Simonnot M-O, Vaughan J, Morel J-L, Echevarria G, Fogliani B, Qiu R-L, Mulligan D (2015) Agromining: farming for metals in the future? Environ Sci Technol 49:4773–4780

van der Ent A, Callahan DL, Noller BN, Mesjasz-Przybylowicz J, Przybylowicz WJ, Barnabas A, Harris HH (2017) Nickel biopathways in tropical nickel hyperaccumulating trees from Sabah (Malaysia). Sci Rep-UK 7:41861

Verbruggen N, Hermans C, Schat H (2009) Molecular mechanisms of metal hyperaccumulation in plants. New Phytol 181:759–776

Visioli G, Gulli M, Marmiroli N (2014) *Noccaea caerulescens* populations adapted to grow in metalliferous and non- metalliferous soils: Ni tolerance, accumulation and expression analysis of genes involved in metal homeostasis. Environ Exp Bot 105:10–17

Welch RM (1981) The biological significance of nickel. J Plant Nutr 3:345–356

White PJ, Broadley MR (2011) Physiological limits to zinc biofortification of edible crops. Front Plant Sci 2:80

Wiersma D, van Goor BJ (1979) Chemical forms of nickel and cobalt in phloem of Ricinus communis. Physiol Plant 45: 440–442

Wood BW, Reilly CC, Nyczepir AP (2004) Mouse-ear of pecan: a nickel deficiency. Hortscience 39:1238–1242

Zhang Q, Smith AF, Sekimoto H, Reid RJ (2001) Effect of membrane surface charge on nickel uptake by purified mung bean root protoplasts. Planta 213:788–793

Zhang X, Houzelot V, Bani A, Morel JL, Echevarria G, Simonnot M-O (2014) Selection and combustion of Ni hyperaccumulators for the phytomining process. Int J Phytoremediat 16:1058–1072

FIGURES AND TABLES

Fig 1. Distribution of the nickel hyperaccumulator plants used in physiological studies.

Fig 2. General mechanisms involved in me t a l hyperaccumulation, which includes (i) stimulated metal absorption in roots; (ii) reduced metal sequestration in root vacuoles; (iii) efficient xylem loading and xylem transport; (iv) strong metal sequestration and compartmentation.

Fig 3. Conceptual model for Ni hyperaccumulation mechanisms processes in hyperaccumulator plants. (i) root uptake; (ii) root sequestration and radial transport; (iii) xylem loading; (iv) xylem transport; (v) xylem unloading; (vi) leaf sequestration; (vii) phloem loading; (viii) phloem translocation; (ix) phloem unloading.

FIGURE 1

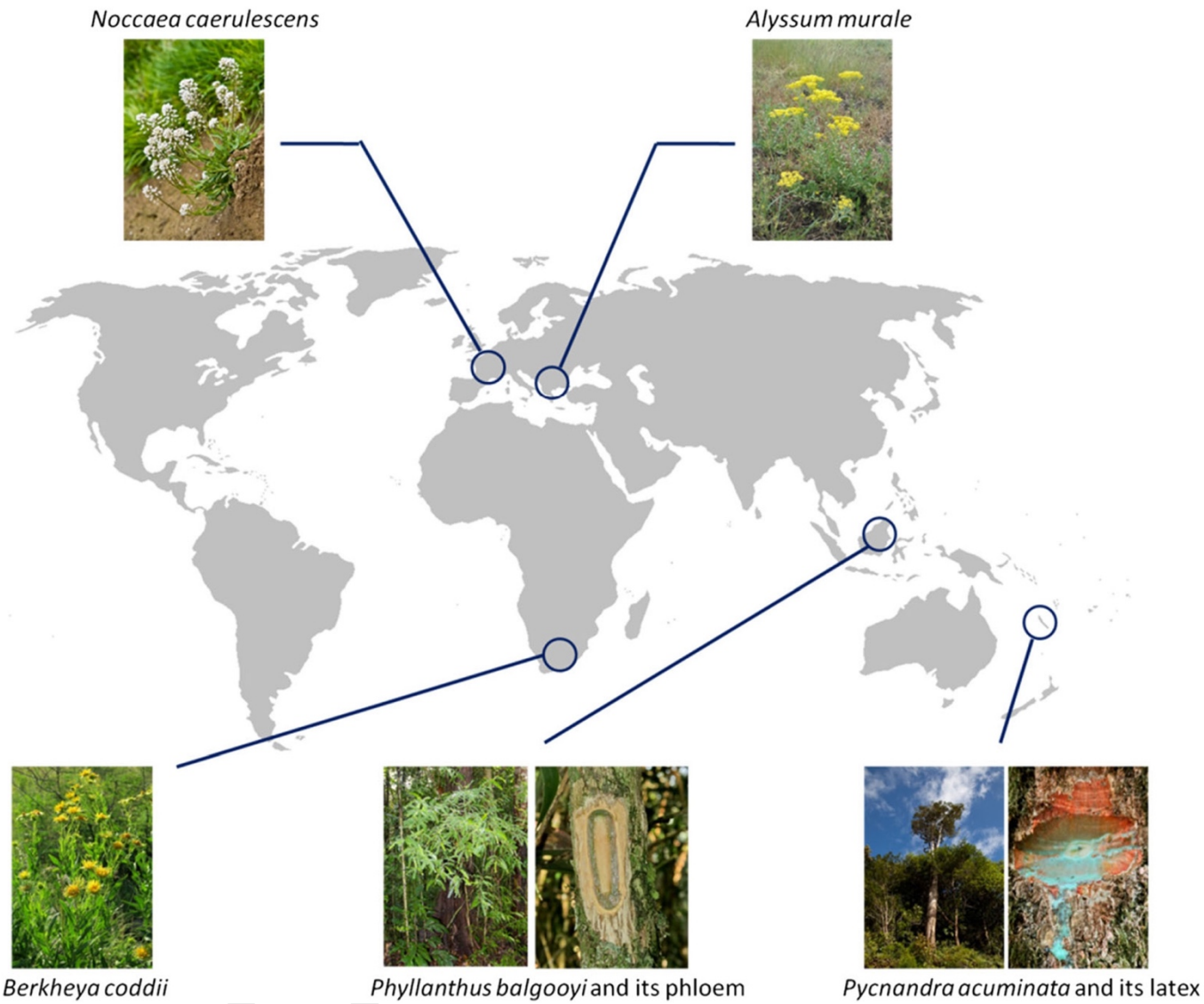

FIGURE 2

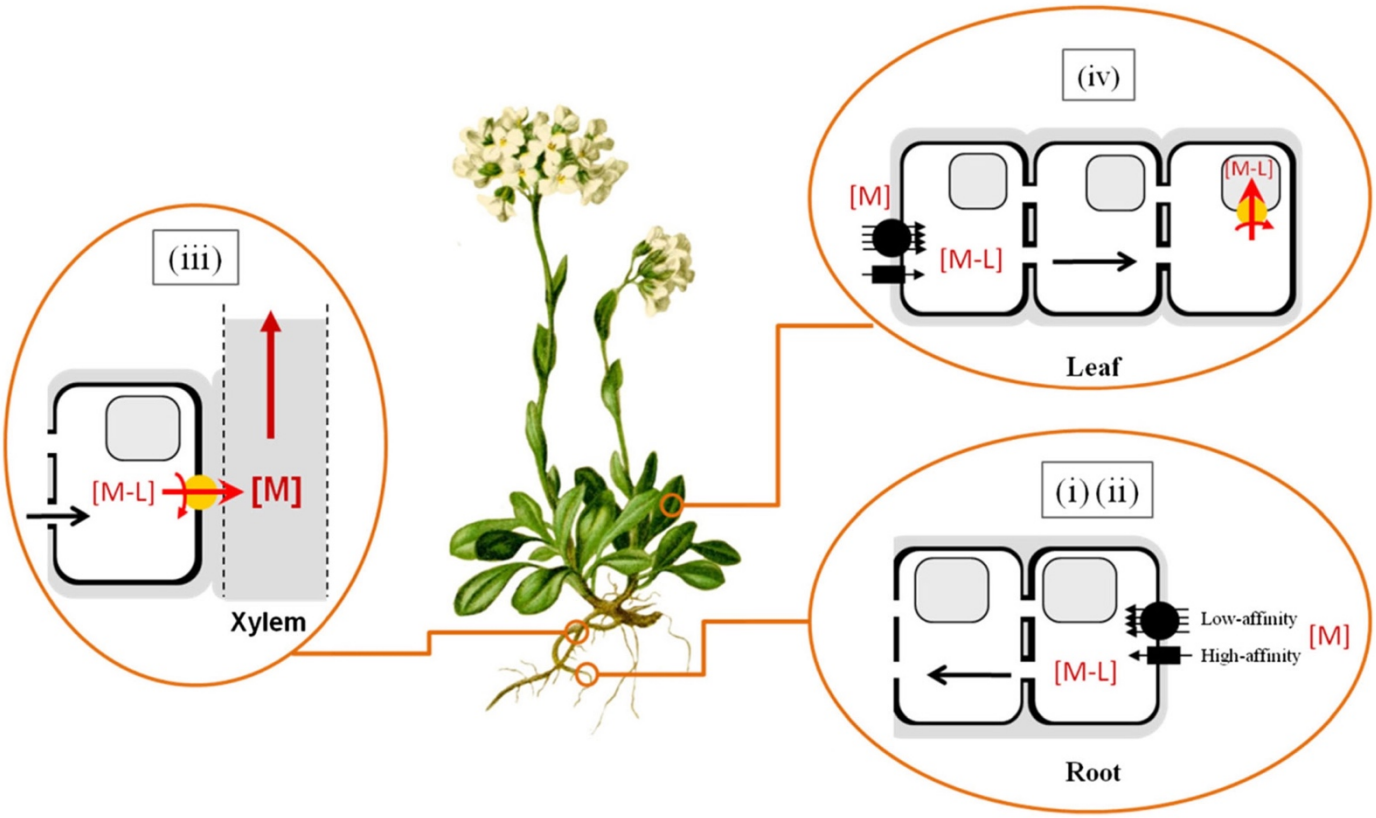

FIGURE 3