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Methylselenized glucose: An efficient organoselenium fertilizer enhancing the selenium content in wheat grains

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ABSTRACT

Selenium (Se) is an essential mineral element for human and other animals, and has been proved to improve plant growth and development and tolerance to different abiotic stresses. Selenium biofortification is considered to be a key strategy to increase the selenium content of edible parts of crops, which is helpful for improving human health. In this work, foliar fertilization with different concentrations and selenium forms was carried out on two wheat varieties at the flowering stage to compare the selenium enrichment effect of Na_2SeO_3, methylselenized selenocysteine (MSC), methylselenized glucose (MSG) and methylselenized lactide (MSL) in wheat grains. Surprisingly, MSG was found to be the preferable fertilizer. After the application of MSG, the highest selenium content in wheat gains reached 6 mg/kg in this experiment, and the average selenium content was 2–4 times *versus* that of Na_2SeO_3 application. Since MSG has high utilization rate and is easily available at relatively low cost, it can be employed as a potential selenium source for selenium biofortification to enhance the added value of agricultural industry.

Owing to their unique chemical- and bio-activities, selenium-containing compounds/materials have been widely employed in catalysis [1–8], medicine [9–11], battery [12,13] and even environment protection [14–17]. In the field of nutrition, selenium is an essential trace element for human beings and other animals. It is incorporated into selenoprotein molecules in the forms of selenocysteine (SeCys) or selenomethionine (SeMet), and plays a very important biological and immune function in organisms [18–20]. Low dietary selenium intake in humans is associated with some health disorders, such as the selenium deficiency (*e.g.*, Keshan disease and Kashin-Beck disease), decreased immune function and reproductive function, increased cancer risks [21]. However, excessive selenium intake may cause selenosis, while the common selenium compounds, such as SeO_2, H_2SeO_3, H_2SeO_4, are always highly toxic. Therefore, dietary selenium supplementation is a topic full of science and technology. Yet, selenium supplementation through food is a relatively safe method. Based on breeding or cultivation practices, improving the available concentration of selenium in the edible part of agricultural crops, *i.e.*, selenium biofortification, is an effective strategy to address dietary nutritional deficiencies [22]. Wheat, rice, corn and other cereals, as agricultural crops for human daily consumption, become an important source of selenium supplementation for selenium deficient people [23]. Wheat is considered to be a suitable choice for selenium biofortification because of its high absorption and enrichment capacity of selenium and high bioavailability of selenium in grains [24].

Selenium fertilization is the most direct and effective way to plant selenium-enriched crops [25]. In the early days, selenium-containing lignite was directly employed as the fertilizer [26], but it would introduce unwanted heavy metals that might pollute the soil after long term use [27]. Inorganic selenium salts, such as Na_2SeO_3 and Na_2SeO_4, can be employed as the foliar fertilizer to avoid the introduction of heavy metal impurities, but their high toxicities hazardous to the environments impede the large-scale applications [28,29]. Organoselenium compounds are relatively low toxic, and selenoaminoacids such as SeCys and SeMet could be employed as feed additives [30,31]. However, the excessive cost makes them difficult to be employed as selenium fertilizer for planting common crops. In our case, we proposed the concept of element-transfer reaction in 2020 [32]. From this point of view, the design of organoselenium fertilizer is just to find an organic material as the carrier of selenium. Carbohydrates were chosen as the ideal carriers due to their low cost as well as the bio-compatible features [33,34]. On this basis, selenized glucose (SG) was developed

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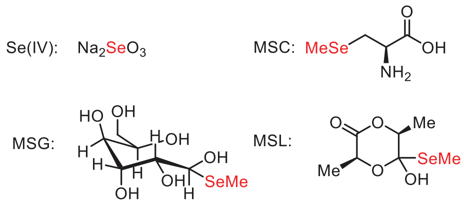

Fig. 1. Abbreviations and chemical structures of the materials employed as selenium fertilizers in this work.

and employed as selenium fertilizer [35] and feed additive [36]. It was also found to effectively inhibit the generation of deoxynivalenol, a harmful mycotoxin produced by *Fusarium graminearum* [37]. Methylselenized glucose (MSG) is the upgraded version of SG. It can be easily prepared *via* the nucleophilic addition reaction of glucose with MeSeMgCl and is now commercially available [38]. In comparison with SG, the end-capping methyl in MSG could significantly enhance the stability of the material [38]. Recently, we unexpectedly found that MSG was a preferable fertilizer for planting selenium-enriched wheat, and its effect was far stronger than that of methylselenized selenocysteine (MSC), methylselenized lactide (MSL) or Na_2SeO_3. Herein, we wish to report our findings.

Four types of materials were employed as selenium fertilizers in this work (Fig. 1): Na_2SeO_3 [Se(IV)] was employed as the representative molecule of inorganic selenium salts. In natural products, selenium exists in the forms of selenoaminoacids, such as SeCys. Therefore, MSC, the methylated SeCys, was employed and this molecule was expected to be more stable than SeCys for the end-capping methyl restraining the oxidation of the free reductive –SeH moiety. MSG, the upgraded version of SG [38], was designed and developed for its good stability in aqueous solution, and testing its activities was our major objective in this work. MSL was prepared *via* the reaction of MeSeMg with L-lactide, similar to the method synthesizing MSG [38]. It was chosen as the candidate because L-lactide being prepared from L-lactic acid was also a bio-compatible molecule [39].

As shown in Table S1 (Supporting information), different selenium treatments exerted obvious influences on the selenium content of wheat grain, depending on the environment, wheat genotype, selenium concentration and selenium form ($P < 0.01$). There were significant interactions between wheat genotype and selenium form/concentration, as well as selenium form/concentration and environment ($P < 0.05$). The interaction between wheat genotype and environment exerted little influence on selenium content in wheat grain ($P > 0.05$).

Environmental factors such as wind, rain and openness may affect the absorption of exogenous selenium by wheat plants. Thus, the selenium content of wheat grains in glasshouse was significantly higher than that in field ($P < 0.01$), because the environmental factors reduced the selenium absorption of wheat by about 50% (Fig. 2, images A and B *vs.* C and D). In our study, two different genotypes of wheat, Zheng9023 and Xi1376, were selected as the examples, which differed in the enrichment abilities for total selenium and selenium forms [40]. Generally, the selenium content in wheat grains of Xi1376 was higher than that of Zheng9023 ($P < 0.01$), *i.e.,* the selenium enrichment ability of Xi1376 was *ca.* 1–2 times *versus* Zheng9023 (Fig. 2, image B *vs.* A), and the differences were further enlarged under field conditions (Fig. 2, image D *vs.* C).

All the selenium fertilizers shown in Fig. 1 could enhance the selenium content in wheat grains (Grain-Se) in a way of gradually going up along with the increasing selenium fertilizer dosages (Fig. 2). The absorption of Na_2SeO_3 by wheat was higher than that of MSC ($P < 0.01$). The effects of the newly designed organoselenium

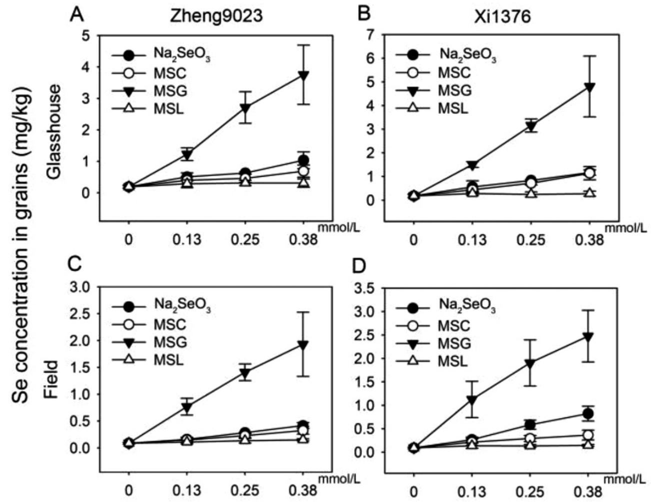

Fig. 2. Tests of the selenium fertilizer candidates in the glasshouse (images A and B) and field (images C and D) with the Zheng9023 (images A and C) and Xi1376 (images B and D) wheats.

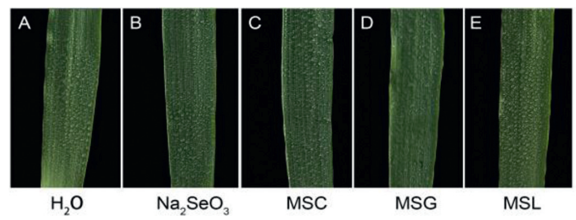

Fig. 3. Drops of the aqueous solutions of the selenium fertilizer candidates adhering to the leaves of Zheng9023.

fertilizers such as MSG and MSL varied greatly. The former was found to be the best fertilizer among the four candidates, while the later showed the poorest effect on selenium enrichment in wheat. Under the glasshouse conditions and using 0.38 mmol/L of MSG as fertilizer, the selenium content in wheat grain could reach 6 mg/kg, *i.e.,* almost 4-5 times (or more) *versus* the same types of wheat grain being planted with Na_2SeO_3, MSC or MSL fertilizer (Fig. 2, images A and B)! Obviously, the priority order of Se-enrichment effects for the four selenium fertilizer candidates was: MSG >> Na_2SeO_4 > MSC > MSL.

During our investigations, it was found that the drops of the aqueous solutions of the selenium fertilizer candidates adhereing onto the wheat leaves were usually round and might easily drip onto the ground, resulting in the waste of the fertilizers (Fig. 3, images A-C, E). However, for MSG, the drops of the aqueous fertilizer could partially infiltrate the leaf surfaces (Fig. 3, image D). It was suggested that the hydroxyls abundantly existing in MSG molecules (Fig. 1) might lead to the interactions (such as the hydrogen bond) with the hydroxyls of cellulose of the leaves to avoid the dripping of the aqueous MSG that could lead to the selenium fertilizer loss. This might partially, if not all, explain the superior performance of MSG to the other three candidates in selenium-enrichment (Fig. 2).

In addition, the excellent performances of MSG for selenium-enrichment of wheat could be explained on the basis of the selenium metabolism and detoxification mechanisms illustrated in Fig. 4, which was adapted and organized from Rayman *et al.* [41], Pilon-Smits and Quinn [42] and White [43]. The methylation of SeCys and SeMet, the reduction of high valence selenium to the insoluble Se(0), and the volatilization of selenium species are considered as detoxification mechanisms for plants to prevent the selenium toxicity [43,44]. On the one hand, whether it is to reduce the

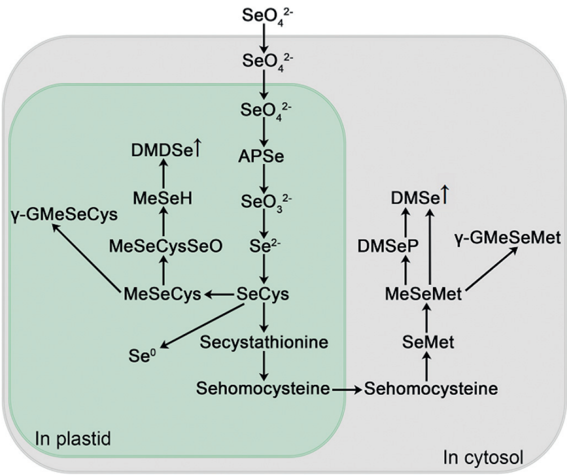

Fig. 4. Generalised process of selenium metabolism and detoxification in plant mesophyll cells.

toxicity of selenium, or to utilize selenium and produce other selenium metabolites, plants need to reduce the high valence selenium species such as Se(VI) or Se (IV) to the low valence Se(0) or Se(−2) [42]. Thus, MSG, as a type of low-valent selenium compound, may be better absorbed by wheat, free of the reduction process. The decomposition of MSG could release MeSe-species, which could participate the synthesis of MeSeCys and MeSeMet directly in plant, so that the progresses might be obviously accelerated. On the other hand, MSG, as a kind of methylated organoselenium compound, may exert fewer influences on plants and is more easily absorbed and accumulated compared with inorganic selenium. However, although MSC and MSL are also methylated organoselenium compounds, they showed poorer effect than Na_2SeO_3 (Fig. 2), which may be caused by other facts such as the solubility as well as the chemical structures of the compounds that may affect their adhering onto the leaves, as being discussed in Fig. 3.

In conclusion, MSG was found to be an excellent selenium fertilizer superior to the traditionally employed inorganic or organic selenium compounds/materials in selenium enrichment ability. In this experiment, the selenium content in wheat grains could be significantly increased up to 6 mg/kg after MSG application, with almost 4–5 times (or more) *versus* the same types of wheat grains being treated with other types of selenium fertilizers. Moreover, toxicity test experiments according to GB 15193.3-2014 showed that the dose of median lethal dose (LD_{50}) of the MSG in mice was 323 mg/kg, indicating that the material was much safer than Na_2SeO_3 ($LD_{50} = 7$ mg/kg). The apparent advantage of MSG in selenium-enrichment of wheat may be attributed to the unique molecule structure containing a lot of hydroxyls and low valent selenium features. The related investigations are ongoing to push forward the applications of MSG.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.cclet.2022.107878.

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