Selenium in wheat from farming to food

Min Wang [2], Baoqiang Li [3], Shuang Li [1], Fanmei Kong [1] *, Xiaocun Zhang [1] *

[1]*College of Resources and Environment, Shandong Agricultural University, No. 61, Daizong Street, Taian, 271018, Shandong Province, China P.R.*

[2] *College of Food Science and Engineering, Shandong Agricultural University, No. 61, Daizong Street, Taian, 271018, Shandong Province, China P.R.*

[3] *Linyi Academy of Agricultural Sciences, No. 351, Wuhe North Street, Lanshan District, Linyi City, 276003, Shandong Province, China P.R.*

[*] *Corresponding author: xczhang@sdau.edu.cn; fmkong@sdau.edu.cn*

Abstract: Selenium (Se) plays an important role in human health. Approximately 80% of the world's population does not consume the recommended Se levels. Wheat is an important staple food and Se source for most people in the world. This article summarizes literatures about Se from 1936 to 2020 to investigate Se in wheat farming soil, wheat, and its derived foods. Selenium fortification and the recommended Se level in wheat were also discussed. Results showed that Se contents in wheat farming soil, grain, and its derived foods were 3.8–552 (mean, 220.99), 0–8,270 (mean, 347.30), and 15–2,372 (mean, 211.86) $\mu g \cdot kg^{-1}$, respectively. Selenium content could be increased by leaf Se fertilizer application, and the contents in grain, flour, and its derived foods could be improved from 93.94 to 1,181.92, 73.06 to 1,007.75, and 86.90 to 587.61 $\mu g \cdot kg^{-1}$ in average. Both Se content in farming soil and grain, foliar Se fertilizer concentration rate and grain Se increased rate showed significant linear relationship. The recommended Se fortification level of wheat in different countries

was calculated in China, India, and Spain, with recorded values of 18.53–23.96, 2.65–3.37, and 3.93–9.88 $g \cdot hm^{-2}$, respectively. Thus, suitable Se fortification in farming effectively improved Se content in wheat grain and its derived foods. Appropriate milling processing and food type are also important factors to be considered to meet people's Se requirement by wheat.

Keywords: Selenium, soil, grain, flour, fortification, bioavailability

Selenium (Se) is a metalloid element of group VI A in the fourth period of the periodic table of the elements. It was first discovered by Swedish scientist Berzelius JJ in 1817 and named it after the Selene, the goddess moon[1]. However, researchers discovered in 1934 that the "alkaline soil disease" and "stumble" of animals were caused by excessive intake of Se. Since then, research on Se has mainly been based on its toxicity[2]. In 1860s, Se was determined as an essential element in animals and human bodies and has gradually gained widespread attention worldwide[3]. Selenium is among the 14 essential trace elements in human body. It is also an important component of Se-containing proteins and enzymes in galacturids[4]. Selenium is closely related to the health, but its total amount in the human body is only 14–20 mg[5]. Selenium deficiency can cause more than 40 kinds of diseases, such as Keshan disease, large bone nodule disease, anemia, infertility, and muscular dystrophy[6]. Moreover, excessive Se intake can cause hair and nail loss, skin ulceration, nerve damage and other toxic symptoms[7]. Therefore, a safe and suitable daily Se intake should be maintained. The range of Se intake recommended by World Health Organization (WHO) is 50–400 μg/day[8]. More than 40 countries in the world lack Se,

and approximately 80% people do not consume the recommended Se intake[9]. In addition, Se bioavailability in human body is not high with values ranging from 10% to 85%[10], and Se can only be ingested through diet. Therefore, an important and long-term task is to improve the Se deficiency situation of people through safe Se-rich diet.

Wheat is the second largest food crop in population consumption[11], and it provides nearly 50% daily calorie intake in most developing countries and more than 70% calorie intake in rural areas[12]. Especially, wheat has a strong ability to enrich Se. It can produce organic Se by absorbing Se in soil or foliage and store them in grains[13]. Selenium is mainly combined with protein in wheat grain and more evenly distributed throughout the whole grain than other minerals[14]. Therefore, a large amount of Se can be stored during grain grinding. Hence, human Se demand can be met through the Se fortification of wheat.

Selenium fortification by wheat is a comprehensive and multi-objective process. Generally, the Se fortification of wheat can be significantly affected by three processes, including grain Se enriching in the field, grain grinding, and wheat-derived food processing. This article summarizes reports related to the Se fortification of wheat to investigate the Se content in farming soil, wheat grain and different wheat derived foods, the effects of field cultivation factors on grain Se content, and food processing on food Se loss. The results provide valuable reference for the suitable amount of leaf fertilizer application rate in field.

2 MATERIALS AND METHODS

2.1 Data collection

The papers relation to Se of wheat grain, flour and wheat derived foods published between 1936 and 2020 were used to set up the database by a literature search using Wiley, ACS, Science Direct, Springer Link and China National Knowledge Infrastructure (CNKI). Search keywords included different combinations, "wheat" or "Selenium" and "flour" or "Selenium" and "food" or "Selenium". Selection criteria included: a) Field experiment: report wheat harvest time, wheat type and fertilization type, including soil pH and Se content; b) wheat milling: report Se fertilizer type and Se content in different components after milling; and c) Food processing: report the source of wheat flour, food type, and Se content in food.

2.2 Data Classification

In selected reports, we summarized these data from soil to grain, milling, then to food under different conditions. A total of 66 research papers and 1066 paired observations were obtained (Figure 1); Grain Se content in different countries came from 42 references (Table S1); Selenium content of different wheat milling components were also obtained under different peeling and flour milling processing were got in 20 papers (Table S2); Selenium content of six kinds of different foods under different flour processing were obtained from 26 reports (Table S3). Total of 117 paired observations for the effects of soil Se on wheat grain from 21 articles, and 188 paired data for the effects of different Se fertilizer on wheat grain from 21 articles were extracted.

2.3 Data management

The database was established using Excel 2019 software. OriginPro 8.5 and PowerPoint 2019 software were used to draw graphics. All statistical analyses were performed using SPSS 18.0 software.

3 RESULTS

3.1 Grain Se content in wheat grain

Selenium content in wheat grain had large variance, which ranged from 0 μg·kg^{-1} to 1,500 μg·kg^{-1} (110.98 μg·kg^{-1} in average) in the world[8,15-50]. The average Se content was lower than that suggested by the reference of Se rich grains (200–300 μg·kg^{-1}[39]). The large variance of Se content in wheat grain was mainly attributed the difference of wheat varieties, area, basic properties of soil, and Se biological strengthening measures in the field.

3.1.1 Variance of Se content among different wheat varieties

Generally, the old and new varieties might have different potentials to accumulate Se in grain. According to our data, grain Se content in wheat reported in 1936–2000 could reach 198.76 μg·kg^{-1} in average, and this value was significantly higher than that in 2001–2020 (Figure 1a). Different wheat varieties own different ability to accumulate Se under the same soil environment. For example, black grain wheat Se content was 177.34 μg·kg^{-1}, which was significantly higher than that in white grain (70.29 μg·kg^{-1})[33].

3.1.2 Grain Se content of wheat in different continents and countries

No significant difference was observed among the average grain Se contents of wheat in Asia[8,15-20,22-25,27-29,31,33-40,43] (63.36 μg·kg^{-1}), Africa[20,22,32,50] (64.15 μg·kg^{-1}),

and Europe[20,22,26,29,30,41,42,44,46,48,50] (85.98 μg·kg^{-1}), and these values which were all lower than the normal level (100 μg·kg^{-1}[39]). A significant difference was observed among the grain Se content in South America[22, 50], North America[20, 22, 47, 49, 50], and Oceania[22, 45, 50] with values of 600.00, 286.23, and 194.80 μg·kg^{-1}, respectively (Figure 2). These values were significantly higher than that in Asia, Africa, and Europe. Grain Se content in different countries on the same continent varied greatly. For Europe, the grain Se content in Spain, Slovakia, Portugal, and Norway varied from 26.75 μg·kg^{-1} to 93.90 μg·kg^{-1}, but that in Italy was 133.44 μg·kg^{-1}.

3.1.3 Basic properties of soil affecting grain Se content of wheat

Soil Se content and pH are the basic properties of soil, and these properties can significantly affect Se content in wheat grain. The total soil Se content varied greatly among different regions. Se-deficient, Se-sufficient, Se-rich, and Se-high soil were considered at soil Se contents of 0–175, 175–450, 450–2,000, and 2,000–3,000 μg·kg^{-1}, respectively[28]. The soil in most parts of the world is Se-deficient. For instance, soil Se contents in Italy, China, India, and South Africa were 130, 21.21 12.60, and 6.14 μg·kg^{-1}, respectively. Globally, soil Se content in farming system range from 10 μg·kg^{-1} to 2,000 μg·kg^{-1} (300 μg·kg^{-1} in average)[51], while that in wheat farming soil is 3.80–552.00 μg·kg^{-1}. Soil Se content had a significant positive correlation with grain Se content (Figure 3). Grain Se content in the soil with Se content of 0–200 μg·kg^{-1} was significantly lower than that in 200–400 and 400-600 μg·kg^{-1}, but no significant difference was observed between that in the soil with Se contents of 200–400 and 400–600 μg·kg^{-1} (Figure 1a).

Soil pH also significantly affects grain Se content in wheat, and a significant difference was observed in wheat grain Se content among neutral soil (pH 6.5-7.5), alkaline soil (pH>7.5), and acid soil (pH<6.5). The grain Se content of wheat planted in neutral soil (pH 6.5–7.5) was the highest (229.42 μg·kg^{-1}), whereas that in acid soil (pH<6.5) was the lowest (55.50 μg·kg^{-1}) (Figure 1a). However, acid soil occupies approximately 30% of the world's ice-free land area and occur mainly in tropical and subtropical regions, and this soil is more likely to be Se-deficient[52].

Therefore, Se-rich soil is an important factor to obtain Se-rich grain. However, most of the soil in the world is Se-deficient, and grain Se content can be effectively improved by artificial fertilization enhancement.

3.1.4 Effects of different Se fertilization on grain Se content in wheat

Se fertilization during wheat planting can significantly increase grain Se content compared with the treatment without Se fertilization. The process of improving grain Se by fertilizer in the field is the most important part in Se fortification. The grain Se contents in wheat around the world since 1936 are summarized in Table S1. The grain Se content of wheat planted in natural soil without Se fertilization treatment ranges from 0 to 1,500.00 μg·kg^{-1} (110.98 μg·kg^{-1} in average)[8, 15–50], and that with Se fertilization treatment ranges from 58.00 μg·kg^{-1} to 8,270.00 μg·kg^{-1} (677.21 μg·kg^{-1} in average). However, significant differences were observed in the effect of different Se fertilizer treatments. Grain Se content with soil Se fertilization treatment ranged from 190.00 μg·kg^{-1} to 6,090.00 μg·kg^{-1} (528.87 μg·kg^{-1} in average)[19, 28, 29, 38, 42, 48, 53], that with foliar Se fertilization treatment ranged from 58.00 μg·kg^{-1} to 8,270.00 μg·kg^{-1}

(729.69 μg·kg^{-1} in average)[8,13,15,16,18-20,23-31,35-38,51,53], and that with seed Se soaking treatment ranged from 64.80 μg·kg^{-1} to 300.00 μg·kg^{-1} (128.67 μg·kg^{-1} in average)[39,54].

Foliar Se fertilization treatment might be the most effective way to improve grain Se content. Grain Se content with foliar Se fertilization treatment was significantly higher than that of soil Se fertilization treatment and CK (Figure 1a). A positive correlation was observed between foliar Se fertilizer application amount and grain Se content growth rate, and this correlation can be expressed with the equation Y=22.20587 x (Figure 4a). The use of foliar Se fertilizer might be more environmentally safe than direct application in soil because of its low concentration in solution, effective absorption, and more accurate control of total Se application. The foliar Se fertilizer is the most popular method in Se fortification. Moreover, Na_2SeO_3 is the most common form of foliar Se fertilizer because of its low toxicity than Na_2SeO_4.

The grain Se content in different countries increased significantly after Se fortification in the field (Figure 4 b), and this value increased from 93.94 μg·kg^{-1} to 1181.92 μg·kg^{-1} after Se fortification. A large variance in effectiveness was observed in different countries. For example, the grain Se content increased in Pakistan, India, Turkey, Spain, South Africa, Norway, Portugal, Slovakia, China, and Italy by 2.16–25.98 times. The grain Se content in Pakistan and Italy increased by 2.16 and 25.98 times, respectively. The differences of fortification effect in these countries might be ascribed to the different Se fertilizer application amount. For example, the wheat Se fertilizer application amount in Italy and China were mostly 120 and 60

$g \cdot hm^{-2}$, respectively, while that in India, Pakistan, Turkey, and South Africa was only 1 $g \cdot hm^{-2}$.

All the reports for Se fertilization indicated that foliar Se fertilization is an effective way to improve the Se content of wheat grain. The most important factor that can affect the effectiveness of Se fertilization for one wheat variety is the Se concentration of the solution. Hence, the determination of the appropriate application amount of foliar fertilizer is the key to the effect of Se nutrient enhancement.

3.2 Selenium in flour and its influencing factors

The proportion of selenium in wheat grains that can be directly ingested by the human body is also a key link for human Se supplementation. Most of the wheat will be ground into flour, which is then made into different foods. Wheat grain is generally divided into bran, embryo, and endosperm, accounting for 14%–16%, 2%–3%, and 81%–84% of the grain weight, respectively[19]. During milling, wheat grains are peeled off. Subsequently, the seed coat, aleurone layer, and embryo are stripped off. Although Se distribution in wheat grain is much more uniform than that of other elements, Se content in bran is approximately three times higher than that in flour after grinding[19, 26, 45]. Bran Se content ranged from 15.00 $\mu g \cdot kg^{-1}$ to 520.00 $\mu g \cdot kg^{-1}$ (149.48 $\mu g \cdot kg^{-1}$ in average)[13, 19, 26, 28, 45], which was significantly higher than that in flour (101.02 $\mu g \cdot kg^{-1}$ in average)[13, 19, 26, 28, 30, 41, 45, 55–66]. Hence, the milling process can result in a part of Se loss.

Different wheat milling methods remarkably affect flour Se content (Figure 1 b). Flour can mainly be divided into two types, namely, whole wheat flour and flour,

according to the milling method. Se content in flour was significantly lower than that in whole wheat flour. According to our results (Table S2), flour Se content ranged from 13.00 μg·kg^{-1} to 500.00 μg·kg^{-1} (101.02 μg·kg^{-1} in average)[13,19,26,28,30,41,45,55-66], and the whole wheat flour Se content ranged from 35.60 μg·kg^{-1} to 650.00 μg·kg^{-1} (227.58 μg·kg^{-1} in average)[26, 56, 61, 63, 65, 67]. Flour road during flour milling can be divided into six flour parts (i.e., three "Broken [B]" and three "Reduced [R]" milling parts) and two kinds of bran parts (i.e., bran and shorts). A significant difference was observed among the ingredients in different flour roads. The flour collected by B1, R1, B2, R2, B3, and R3 was standard flour, the flour collected by B1, R1, B2, and B3 was bread flour, and the flour from B1 and R1 was refined flour[45]. Flour road schematic diagram of Bühlermlu-202 mill and Se content of flour in each flour road is shown in Figure 5. The Se content in different components after wheat milling can be arranged as follows: Bran> B flour >R flour. The Se contents of flour from R1, R2, R3, B1, B2, and B3 were 66.42, 65.73, 68.98, 71.59, 81.52, and 77.94 μg·kg^{-1} in average, respectively. The Se content of flour in common flour roads was B3>B2>R3>R1>R2>B1. The rate of Se concentration loss and Se content loss in wheat milling were 17.19% and 46.40%, respectively. Most of the published literature used Se concentration loss, and a few studies have focused on Se content loss. The peeling rate of 4%–5% can effectively increase flour Se content. When the peeling rate was greater than 9%, no significant difference was observed in the Se content between flour and unpeeled flour[19].

Field biofortifications can significantly increase Se content in flour and have

significant effects on Se content in each flour road. After Se fortification, Se content increased from 227.58 μg·kg^{-1} to 1,110.03 μg·kg^{-1} in whole wheat flour and from 101.02 μg·kg^{-1} to 714.90 μg·kg^{-1} in flour, respectively. Se contents in foliar fortified whole wheat flour and foliar fortified flour were significantly higher than those in whole wheat, soil fortified, and unfortified flour (Figure 1b). The Se content in flour roads after field biofortifying can be arranged as B2>R3>B1>R2>R1, which was quite different with that of common flour. The average rates of Se concentration and content loss in wheat milling were 15.04% and 38.56%, respectively, after Se fortification.

Therefore, milling methods might affect flour Se content.

3.3 Selenium in wheat derived foods

Flour is generally used for the preparation of foods, such as bread, noodles, and biscuits. These staple foods play an important role in people's diet. For example, wheat-related traditional foods account for 75% of the total wheat consumption in China[34]. Se content in most wheat-derived foods is in normal range according to the data over the past 50 years. Se content in foods ranged from 3.60 μg·kg^{-1} to 1130.00 μg·kg^{-1} with an average of 191.87 μg·kg^{-}[113,30,41,45,46,56,58-61,63-66,68-79]. Se content in different wheat-derived foods were significantly different (Figure 6), and Se content in cooking foods was 382.83 μg·kg^{-1}, which was significantly higher than that in baked foods (244.98 μg·kg^{-1}). The average Se contents in pasta, noodles, biscuits, and bread were 325.45, 251.53, 181.65, and 137.51 μg·kg^{-1}, respectively.

High temperature can result in the volatilization of Se. Hence, Se loss in food

processing is mainly lost during heating. Especially, Se loss is high under the dual effect of dissolution and heat volatilization when cooking, steaming, and frying the same food[80,81].

Hence, boiling, baking, or other food processing methods will lead to Se loss in food. Moreover, soaking steps in food fermentation will reduce food Se content, but it is easily affected by foods species, such as Se content in mung bean and millet decreased in soaking[80]. The change of Se content after wheat food fermentation has not been study, but its possibility is not excluded.

In addition, field Se fortification can significantly increase Se content in wheat-derived foods (Figure 1c). For example, Se content in pasta increased from 22.4 $\mu g \cdot kg^{-1}$ to 424.43 $\mu g \cdot kg^{-1}$ (17.94 times) and that in bread increased from 119.15 $\mu g \cdot kg^{-1}$ to 644.69 $\mu g \cdot kg^{-1}$ (4.41 times). Se content in food is also related to the amount of Se fertilizer. Hart et al[56]. found that foliar Se application rate is positively correlated with bread Se content, and it can be expressed using the formula Y=19.2262 X+95.95332.

Food processing is an important factor that affects Se content in food. Moreover, field Se fortification is an effective way to increase Se content in wheat-derived foods.

3.4 Selenium bioavailability

Not all the Se content obtained from foods can be used by the human body. The ratio of body absorbed Se to total intake Se is called bioavailability[10]. The Se from food can be effectively used by the human body only absorbed in blood circulation or tissues and transformed into active substances. A large difference was observed for

the bioavailability of different Se types. Selenium types in foods include inorganic Se (i.e., selenite) and organic Se (i.e., SeMet). Selenium mainly exists in the form of SeMet in wheat grain, flour, and food, and it accounts for 70%-90%[14,82], 59%-82%[43,76,83,84], and 42%-83%[43,56,83] of total Se, respectively.

Different Se types are digested and absorbed in different ways, causing difference in bioavailability. Organic Se is mainly actively absorbed by human small intestine, in which bioavailability generally fluctuates between 70%–90%[10, 73]. Inorganic Se absorption modes occur via simple absorption (selenite) and passive diffusion (selenite), in which bioavailability is generally less than 50%. Moreover, the long-term consumption of inorganic Se might result in toxic and side effects[10]. The molecular of H_2Se is the key to human body's Se metabolism. The role of H_2Se mainly includes two aspects[85, 86]: 1) H_2Se first transforms to selenite and SeMet form, and then synthesizes selenoprotein in liver and 2) SeMet and SeMeCys catalyze H_2Se to form different Se ions forms under continuous methylation, which are discharged through respiration, urine, and sweat.

Se bioavailability in the human body can be predicted via *in vitro* simulated gastrointestinal digestion model[87], Caco-2 based cell model[88], animal models[89], and human Se bioavailability detection[90]. Selenium bioavailability in wheat was 83% in rat feeding trials, while those in mushroom, tuna, and beef kidneys were 5%, 57%, and 97%, respectively[89]. Selenium bioavailability in wheat flour was also very high, with values ranging from 75.4% to 91.8%. The consecutive consumption of Se-enriched wheat for six weeks could significantly increase human serum Se content,

but Se-enriched fish had no obvious effect[90]. Generally, SeMet can be effectively absorbed by the human body, in which bioavailability may exceed 90%. By using *in vitro* gastrointestinal digestion method to simulate bread digestion, soluble Se content after gastric and gastrointestinal digestion accounted for 75% and 89% of total Se content in bread, respectively, in which SeMet content accounted for 95% and 96.8% of soluble Se[91].

Selenium bioavailability in foods ranged from 10% to 85%[10]. These differences in bioavailability might be ascribed to the following factors: 1) selenium type in food - different Se types showed different bioavailability, for instance, SeMet and SeMeCys have a bioavailable of up to 90%, while selenates and selenite have a bioavailability of up to 50%[89]. 2) food type - a high-fat diet can hinder Se absorption, resulting in low Se bioavailability[87]. 3) food processing - heat treatment not only affects total Se content but also reduced Se antagonist content. However, proper heat treatment might improve Se bioavailability[89]. 4) antagonism with other minerals - Ca intake in the human body would reduce Se bioavailability. Meanwhile, Vc could transform selenates into insoluble Se compounds in a short time, thus reducing Se bioavailability[92]. 5) digestion and absorption capacity of human body - for instance, gastrointestinal diseases will reduce Se bioavailability.

Despite the numerous influencing factors, Se can be supplemented to the human body through wheat-related foods, because Se bioavailability in wheat is relatively high (75.4%–91.8%).

3.5 Suitable level of Se in wheat grain and in fertilizer applied in the field

Considering that both insufficient and excessive Se intake will have adverse effects on human health, a suitable and safe amount of Se intake should be maintained. The range of Se intake recommended by WHO is 50–400 μg/day. Inorganic Se has a strong potential toxicity to the human body. Hence, the supplement of organic Se in food is the first choice. Se-rich wheat might be an ideal popular food to improve Se in the human body because of its relatively stable intake, high ability to accumulate Se, and high Se bioavailability. Field Se fortification can effectively improve grain Se content in wheat and then obtain the Se-rich wheat-derived foods.

Dietary pattern, which refers to the combination of various forms of food ingredients used in people's actual life, should also be considered[93, 94]. The representative dietary patterns are divided into Western, Oriental, and Mediterranean dietary patterns. Western dietary patterns are mainly characterized by the intake of large amounts of red meat, processed meat products, refined cereals, desserts, French fries, and high-fat dairy products. Oriental dietary patterns are mainly characterized by the intake of a large number of fruits, vegetables, legumes, whole wheat, an appropriate amount of fish, and poultry. Mediterranean dietary patterns are mainly characterized by the intake of monounsaturated fatty acids rich in olive and olive oil, whole grains, fruits, vegetables and dairy products, weekly intake of fish, poultry, nuts, and legumes. The distribution law of food Se content is as follows[61]: fish > meat > egg > cereal > fruits and vegetables. Hence, the actual Se intake per capita in western dietary patterns countries could reach the recommended level. The actual Se intake per capita in some Mediterranean dietary pattern countries could reach the

recommended level such as Italy, but some countries such as Spain cannot not reach the recommended level. Interestingly, the actual Se intake per capita in Oriental dietary patterns countries, such as China and India, did not reach the recommended level.

With wheat as Se source, the level of Se needed in wheat grains and the amount of Se to be applied in the field should be determined.

According to the recommended daily Se intake per capita, actual Se intake per capita, total Se loss rate, the proportion of Se in cereals in daily Se intake and flour Se content, daily insufficient Se intake, and suitable Se fortification level by wheat could be calculated to determine whether Se is deficient in the region and to calculate the appropriate Se fertilizer amount for biofortification.

In China, according to the national nutrition and health guidelines, the recommended Se intake per capita is 60–400 $\mu g \cdot day^{-1}$, the recommended Se in grain is 150 g (assuming all for wheat), the actual Se intake is 43.90 $\mu g \cdot kg^{-1}$, and grain daily Se intake accounts for approximately 22.6%. The upper limit of Se content in wheat grain is 300 $\mu g \cdot kg^{-1}$ in China, and the scope of Se content in wheat grain is 242.74–300.00 $\mu g \cdot kg^{-1}$. According to the formula and the parameters, the amount of Se fortification by foliar Se fertilizer in China should be 18.53–23.96 $g \cdot hm^{-2}$ to meet people's daily need. Thus, the amount of Se fortification should be 2.65–3.37 and 3.93–9.88 $g \cdot hm^{-2}$ in India and Spain, respectively (Figure 7, Table 1[8, 92, 95–100]).

Table 1 Recommended amount of wheat selenium fertilizer in different countries

Dietary pattern	Country	Recommended daily Se intake per capita (μg·d^{-1})	Wheat grain Se content (μg·kg^{-1})	Actual Se intake per capita (μg·d^{-1})	Recommended wheat grain Se content (μg·kg^{-1})	Recommended Se fertilizer applying amount (g·hm^{-2})
Oriental dietary patterns	China	60.00[100]	47.46	43.90[97]	242.74-300.00	18.53-23.96
	India	50.00[8]	171.70	48.00[98]	272.76-300.00	2.65-3.37
Mediterranean dietary patterns	Spain	50.00[8]	93.90	49.24[95]	175.84-300.00	3.93-9.88
	Italy	50.00[8]	133.44	66.53[96]	No need to fortification	No need to fortification
Western dietary patterns	Australia	55.00[92]	191.83	57.0[99]	No need to fortification	No need to fortification
	America	55.00[92]	304.95	80.00[98]	No need to fortification	No need to fortification

4 Future trends

The enhancement of Se nutrition to human body by wheat involves many processes, such as acquisition of Se-rich wheat grains, reduction of Se loss in the process of flour milling and food processing, and improvement of Se bioavailability in food.

Wheat varieties and their corresponding Se fortification cultivation measures are both important to obtain Se-rich grain. The development of wheat variety with high potential ability to accumulate Se in grain is needed. Variety with potential high Se accumulation can save limited Se fertilizer resources and obtain an ideal Se enrichment effect. Conventional wheat breeding and modern biotechnology methods should be used to breed Se-rich wheat variety. The detection and use of Se-rich gene existing in wheat and its relatives should also be considered. Other nutrient influence on Se utilization needs to be detected. This field should be further studied. Se enhancement measures in the field also need to be updated according to the change of

cultivars and cultivation environment, and further investigation is required.

For the reduction of Se loss during flour milling and food processing, the mechanism of the effects on Se loss in different food processing methods should be focused on. The improvement of Se bioavailability in food is a very complicated task.

If the metabolism of different forms of Se in body and the interaction mechanism with other substances are well understood, the addition of food additives to improve Se bioavailability or Se products with high bioavailability to directly increase Se content in food can be considered. This process should also be considered in the food industry.

Selenium deficiency is a worldwide problem, and its fortification should strengthen international cooperation through international schemes such as Harvest Plus. Moreover, we should raise public awareness of the dangers of Se deficiency to obtain as much support as possible, such as sustained funding from local government.

In summary, suitable Se fortification, appropriate processing, reasonable food type, international collaboration, and government support are all important to meet people's Se requirements through wheat.

5 Author contributions

All authors contributed to writing the article.

6 Competing interests

The authors declare no competing interests.

7 References

1. Schwarz, K. & Foltz, C. M., Selenium as an integral part of factor 3 against

dietary necrotic liver degeneration. *J Am Chem Soc.* **79**, 3292 (1957).

2. Zhang, J. J., The Biological functions of selenium and research development of se-enriched foodstuff. *Studies of Trace Elements and Health.* ***23***, 58-60 (2006).

3. Kilness, A. W., Selenium and public health. *South Dakota Journal of Medicine.* **26**, 17 (1973).

4. Arteel, G. E. & Sies, H., The biochemistry of selenium and the glutathione system. *Environ Toxicol Phar.* **10**, 153 (2001).

5. Huang, Q. J., Wang, S. S. & Zheng, W., Research progress of selenium enrichment in Wheat. *Journal of Green Science and Technology.* **12***,* 73-76 (2015).

6. Rayman, M. P., The importance of selenium to human health. *The Lancet.* **356**, 233 (2000).

7. U, C. I. O. M., *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids*. (2000).

8. Liu, H., Yang, Y. & Wang, C. H., Selenium content of wheat grain and its regulation in different wheat production regions of china. *Scientia Agricultura Sinica.* **49**,1715-1728 (2016).

9. Rita, Stoffaneller, Nancy, L. & Morse., A review of dietary selenium intake and selenium status in Europe and the Middle East. *Nutrients.* (2015).

10. Li, Y. N., Ma, L.Y. & Huang, K. L., Research advancement on bioavailability of selenium in dietary sources. *Food and Nutrition in China.* **25**, 5-9 (2019).

11. Cardoso, R. V. C., Fernandes, Â., Gonzaléz-Paramás, A. M., Barros, L. & Ferreira, I. C. F. R., Flour fortification for nutritional and health improvement: A review. *Food*

Res Int. **125**, 108576 (2019).

12. Cakmak, I., Enrichment of cereal grains with zinc: Agronomic or genetic biofortification? *Plant Soil.* **302**, 1 (2008).

13. Wang, P., Zhang, X. C. & Kong, F. M., Change research of selenium in the processing from grain to steamed bread. *Current Biotechnology.* **6**, 422-427 (2016).

14. Cubadda, F. *et. al.*, Changes in selenium speciation associated with increasing tissue concentrations of selenium in wheat grain. *J Agr Food Chem.* **58**, 2295 (2010).

15. Wang, M., Ali, F., Wang, M., Dinh, Q. T. & Liang, D., Understanding boosting selenium accumulation in Wheat (Triticum aestivum L.) following foliar selenium application at different stages, forms, and doses. *Environ Sci PPollutr.* 27 (2020).

16. Zhang, P. P., Ma, H. X. & Yao, J. B., Effects of selenium foliar spray on selenium distribution in milling fractions in common wheat. *Journal of Nuclear Agricultural Sciences.* **33**, 2254-2260 (2019).

17. Qin, C., Shi, C. & Wan, Q. Y., Speciation analysis of selenium in selenium-enriched wheat by PLC-ICP-MS. *Food Research And Development.* **40**, 140-144 (2019).

18. Dong, S. F., Sun, M. & Zhao, J. M., Effects of sodium selenite application at anthesis stage on the growth characteristics and Se accumulation in wheat plants. *Journal of Shanxi Agricultural University (Natural Science Edition).* **39**, 13-18 (2019).

19. Chen, B. N., *Huazhong Agricultural University.* (2019).

20. Zou, C. *et. al.*, Simultaneous biofortification of wheat with Zinc, Iodine,

Selenium, and Iron through foliar treatment of a micronutrient cocktail in six countries. *J Agr Food Chem.* **67**, 8096 (2019).

21. López-Bellido, F. J., Sanchez, V., Rivas, I., López-Bellido, R. J. & López-Bellido, L., Wheat grain selenium content as affected by year and tillage system in a rainfed Mediterranean Vertisol. *Field CroP Res.* **233**, 41 (2019).

22. Ji, H. T., Wang M. & Cao, Y., Correlation analysis of Fe, Zn, Se mass fraction in Durum and Emmer Wheat. *Acta Agriculturae Boreali-occidentalis Sinica.* **27**, 772-778 (2018).

23. Wang, J. M., Chen, H. Y. & Guo, J. J., *Journal of Yangtze University (Natural Science Edition).* **15**,1-4 (2018).

24. Feng, K., Jia, L. L. & Jia, Y. H., Effect of selenium application on yield and selenium content of spring wheat under different plantin. *Journal of Triticeae Crops.* 7 (2018).

25. Jin, Y. F. & Gao, B. D., Effect of selenium fertilizer on Se-enrich reaction and Se absorption and distribution of spring wheat. *Soil and Fertilizer Sciences.* **274**, 113-117 (2018).

26. De Vita, P. *et. al.*, Selenium-enriched durum wheat improves the nutritional profile of pasta without altering its organoleptic properties. *Food Chem.* **214**, 374 (2017).

27. Zhang, R., Liu, M. M. & Wang, R. H., Effect of foliar spraying of plant Se-nutrients on wheat yild and quality. *Journal of Triticeae Crops.* **35**, 856-859 (2015).

28. Yu, R., *Northwest A&F University.* (2015).

29. Catarina Galinha, M. S. A. M., Characterization of selenium-enriched wheat by agronomic biofortification. *Journal of Food Science & Technology.* **52**, 4236 (2015).

30. Poblaciones, M. J., Rodrigo, S., Santamaría, O., Chen, Y. & McGrath, S. P., Agronomic selenium biofortification in Triticum durum under Mediterranean conditions: From grain to cooked pasta. *Food Chem.* **146**, 378 (2014).

31. Meng, L. M., Yang, Z. G. & Zhang, K., Effect of application of race element fertilizer on wheat yield and content of trace elements. *Journal of Anhui Agricultural Sciences.* **14**, 4283-4285 (2014).

32. Beladel, B. *et. al.*, Selenium content in wheat and estimation of the selenium daily intake in different regions of Algeria. *Appl Radlat Isotopes.* **71**, 7 (2013).

33. Pei, Z. Y., Wen, H. Q. & Zhang, L. S., Study on rich selenium black kernel wheat donghei No.1. *Seed.* **32**, 74-76 (2013).

34. Wang, X.X., Jia, A. X. & Yu, Z. L., Distribution of mineral elements in wheat milling. *Modern Flour Milling Industry.* **26**, 23-26 (2012).

35. Zhang, X., Bu, D. N. & Li, R. N., Effects of foliar spraying microelement fertilizers on yield and quality of winter wheat. *Journal of Triticeae Crops.* **32**, 747-749 (2012).

36. Zhang, J. Y., Zhang, P. P. & Ma, H. X., Effects of spraying micronutrients on yield,quality and micronutrient content in grain of wheat. *Acta Agriculturae Jiangxi.* **24**, 64-66 (2012).

37. Zhang, Y., Effects of selenium and zinc fertilizer on yield and selenium

absorption and accumulation in spring wheat. *Guangxi Agricultural Sciences.* **43**, 626-629 (2012).

38. Tang Y. X., Wang, H. M. & Yang, J. F., Studies on the selenium content and selenium enriched technique of winter wheat in hebei province. *Journal of Triticeae Crops.* **31**, 347-351 (2011).

39. Tang, Y. X., Wang, H. M. & Lv, Y. H., Effects of selenium seed soaking on growth, yield and seeds selenium content of wheat. *Journal of Triticeae Crops.* **30**, 731-734 (2010).

40. Lu, L., Ji, Y. M. & Li, L. R., Analysis of Fe, Zn and Se contents in different wheat cultivars (Lines) planted in different areas. *Chinese Journal of Applied & Environmental Biology.* **16**, 646-649 (2010).

41. Cubadda, F., Aureli, F., Raggi, A. & Carcea, M., Effect of milling, pasta making and cooking on minerals in durum wheat. *J Cereal Sci.* **49**, 92 (2009).

42. Ducsay, L., Ložek, O. & Varga, L., The influence of selenium soil application on its content in spring wheat. *Plant Soil & Environment.* **55**, 80 (2009).

43. Yadav, S. K., Singh, I., Sharma, A. & Singh, D., Selenium status in food grains of northern districts of India. *J Environ Manage.* **88**, 770 (2008).

44. Spadoni, M. *et. al.*, Bioaccessible selenium in Italian agricultural soils: Comparison of the biogeochemical approach with a regression model based on geochemical and pedoclimatic variables. *Sci Total Environ.* **376**, 160 (2007).

45. Lyons, G., Ortiz-Monasterio, I., Stangoulis, J. & Graham, R., Selenium concentration in wheat grain: Is there sufficient genotypic variation to use in breeding?

Plant & Soil. **269**, 369 (2005).

46. Díaz-Alarcón, J. P., Navarro-Alarcón, M., de la Serrana, H. L. & López-Martínez, M. C., Determination of selenium in cereals, legumes and dry fruits from southeastern spain for calculation of daily dietary intake. *Sci Total Environ.* **184**, 183 (1996).

47. Wyatt, C. J., Meléndez, J. M., Acu A, N. & Rascon, A., Selenium (Se) in foods in northern Mexico, their contribution to the daily Se intake and the relationship of Se plasma levels and glutathione peroxidase activity. *Nutr res.* **16**, 949 (1996).

48. Tveitnes, S., Singh, B. R. & Ruud, L., Selenium concentration in spring wheat as influenced by basal application and top dressing of selenium-enriched fertilizers. *Fertilizer Research.* **45**, 163 (1995).

49. Harn, M. H., Kuennen, R. W., Caruso, J. A. & Fricke, F. L., Determination of trace amounts of selenium in corn, lettuce, potatoes, soybeans, and wheat by hydride generation/condensation and flame atomic absorption spectrometry. *J Agr Food Chem.* **29**, 792 (1981).

50. Robinson, W. O., Selenium content of wheat from various parts of the world. *Ind. Eng. Chem* **6**, 736 (1936).

51. Galinha, C. *et. al.*, Determination of selenium in bread-wheat samples grown under a Se-supplementation regime in actual field conditions. *Journal of Radioanalytical & Nuclear Chemistry,* **291**, 231 (2012).

52. Von Uexküll, H. R. & Mutert, E., Global extent, development and economic impact of acid soils. *Springer Netherlands.* (1995).

53. Wang, J. W., *Northwest A&F University.* (2012).

54. Souza, G. A. *et. al.*, Genotypic variation of zinc and selenium concentration in grains of Brazilian wheat lines. *Plant Sci.* **224**, 27 (2014).

55. Li, X. Z., Wang, X. X. & Ma, S., Effect of wheat peeling technology on selenium content in flour. *Cereals & Oils.* **30**, 50-54 (2017).

56. Hart, D. J. *et. al.*, Selenium concentration and speciation in biofortified flour and bread: Retention of selenium during grain biofortification, processing and production of Se-enriched food. *Food Chem.* **126**, 1771 (2011).

57. Matos-Reyes, M. N., Cervera, M. L., Campos, R. C. & De la Guardia, M., Total content of As, Sb, Se, Te and Bi in Spanish vegetables, cereals and pulses and estimation of the contribution of these foods to the Mediterranean daily intake of trace elements. *Food Chem.* **122**, 188 (2010).

58. Wang, H. B., Li, Q. L. & Liu, J. L., Development of kappa-selenocarrageen in premix and determination of se content in wheat flour and its products. *Cereal & Feed Industry.* **6**, 5-8 (2008).

59. Alamin, M. B., Bejey, A. M., Kučera, J. & Mizera, J., Determination of mercury and selenium in consumed food items in Libya using instrumental and radiochemical NAA. *J Radioanal Nual Chem.* **270**, 143 (2006).

60. Klapec, T., Mandi, M. L., Grgi, J., Primorac, L. & Krstanovi, V., Selenium in selected foods grown or purchased in eastern Croatia. *Food Chem.* **85**, 445 (2004).

61. Murphy, J. & Cashman, K. D., Selenium content of a range of Irish foods. *Food Chem.* **74**, 493 (2001).

62. Díaz-Alarcón, J. P., Navarro-Alarcón, M., de la Serrana, H. L. & López-Martínez,

M. C., Determination of selenium in cereals, legumes and dry fruits from southeastern Spain for calculation of daily dietary intake. *Sci Total Environ.* **184**, 183 (1996).

63. Barclay, M. N. I., MacPherson, A. & Dixon, J., Selenium Content of a Range of UK Foods. *J Food Compos Anal.* **8**, 307 (1995).

64. Oster, O. & Prellwitz, W., The daily dietary selenium intake of West German adults. *Biol Trace Elem Res.* **20**, 1 (1989).

65. Arthur, D., Selenium Content of Canadian Foods. *Canadian Institute of Food Science and Technology Journal.* **5**, 165 (1972).

66. Madaric, A., Kadrabova, J. & Ginter, E., The selenium content of selected food from the Slovak Republic. *Food Chem.* **58**, 29 (1997).

67. Gao, X. Y., Gao, Q. Z. & Zhu, Y. R., Determination oftrace selenium content in nanyang color wheat. *Science and Technology of Cereals,Oils and Foods.* **23**, 67-70 (2015).

68. He, Y., The development and antioxidation of selenium rich biscuits. *The Food Industry.* **40**, 153-157 (2019).

69. Zhai, L. G., Li, L. J. & Guo, Y. X., Development of selenium-enriched rye crisp biscuit. *Cereal & Feed Industry.* **11**, 29-33 (2018).

70. Wang, X. Y & Zhang, Q. F., The development of nutrition rich selenium yeast bread. *Cereals Oils.* **28**, 25-27 (2015).

71. Bryszewska, M. A. *et. al.*, The effect of consumption of selenium enriched eye/wheat sourdough bread on the body's selenium status. *Plant Food Hum Nutr.* **62**, 121 (2007).

72. Pappa, E. C., Pappas, A. C. & Surai, P. F., Selenium content in selected foods from the Greek market and estimation of the daily intake. *Sci Total Environ.* **372**, 100 (2006).

73. Holben, D. H. & Smith, A. M., The diverse role of selenium within selenoproteins: a review. *Journal of the American Dietetic Association*. **99**, 836 (1999).

74. Finley, J. W., Matthys, L., Shuler, T. & Korynta, E., Selenium content of foods purchased in North Dakota. *Nutr Res.* **16**, 723 (1996).

75. Aro, A., Kumpulainen, J., Alfthan, G., Voshchenko, A. V. & Ivanov, V. N., Factors affecting the selenium intake of people in Transbaikalian Russia. *Biol Trace Elem Res.* **40**, 277 (1994).

76. Eurola, M. H., Ekholm, P. I. S. H., Ylinen, M. E., Varo, P. T. & Koivistoinen, P. E., Selenium in Finnish foods after beginning the use of selenate-supplemented fertilisers. *J Sci Food Agr.* (1991).

77. Olson, O. E. & PALMER, I. S., Selenium in foods purchased or produced in south dakota. *J Food Sci.* **49**, 446 (1984).

78. Ferretti, R. J. & Levander, O. A., Effect of milling and processing on the selenium content of grains and cereal products. *Journal of Agricultural & Food Chemistry.* **22**, 1049 (1974).

79. Laila, Hussein, And, J & Bruggeman, Selenium analysis of selected Egyptian foods and estimated daily intakes among a population group. *Food Chem.* (1999).

80. Guo, H., Huang, X. S,. Hui, J. R,. Chen, Y. H. & Shen, Q, Effect of processing on

selenium content of wheat. *Food Science and Technolog.* **42**, 185 (2017).

81. Khanam, A. & Platel, K., Influence of domestic processing on the bioaccessibility of selenium from selected food grains and composite meals. *Journal of Food Science and Technology.* **53**, 1634 (2016).

82. Kirby, J. K., Lyons, G. H. & Karkkainen, M. P., Selenium speciation and bioavailability in biofortified products using species-unspecific isotope dilution and reverse phase ion pairing-inductively coupled plasma-mass spectrometry. *Journal of Agricultural & Food Chemistry.* **56**, 1772 (2008).

83. Hawkesford, M. J. & Zhao, F., Strategies for increasing the selenium content of wheat. *J Cereal Sci.* **46**, 282 (2007).

84. D Az Huerta, V., Hinojosa Reyes, L., Marchante-Gay N, J. M., Fern Ndez S Nchez, M. A. L. & Sanz-Medel, A., Total determination and quantitative speciation analysis of selenium in yeast and wheat flour by isotope dilution analysis ICP-MS. *J Anal Atom Spectrom.* **18**, 1243 (2003).

85. Wrobel, J. K., Power, R. & Toborek, M., Biological activity of selenium: Revisited. *International Union of Biochemistry and Molecular Biology Life.* **68**, 97 (2016).

86. Gerald, F. C., Biomarkers of Selenium Status. *Nutrients.* **7**, 2209 (2015).

87. Shen, L., Van Dyck, K., Luten, J. & Deelstra, H., Diffusibility of selenate, selenite, seleno-methionine, and seleno-cystine during simulated gastrointestinal digestion. *Biological Trace Element Research.* **58**, 55 (1997).

88. Artursson, P. & Karlsson, J., Correlation between oral drug absorption in humans

and apparent drug permeability coefficients in human intestinal epithelial (Caco-2) cells. *Biochem Bioph Res CO.* **175**, 880 (1991).

89. Thomson, C. D., Assessment of requirements for selenium and adequacy of selenium status: a review. *EurJ Clin Nutr.* **58**, 391 (2004).

90. Meltzer, H. M. *et al.*, Different bioavailability in humans of wheat and fish selenium as measured by blood platelet response to increased dietary Se. *Biol Trace Elem Res.* **36**, 229 (1993).

91. Sánchez-Martínez, M., Pérez-Corona, T., Cámara, C. & Madrid, Y., Preparation and Characterization of a Laboratory Scale Selenomethionine-Enriched Bread. Selenium Bioaccessibility. *J Agric Food Chem.* **63**, 120 (2015).

92. Rahavi, E. B., Altman, J. M. & Stoody, E. E., *Dietary Guidelines for Americans, 2015-2020: National Nutrition Guidelines*. (2019).

93. Cheng, M. W., *National Institute for Nutririon and Health, Chinese Center for Diseases Control and Preventio*n. (2017).

94. Zhang, J. G., *Chinese Center for Disease Control and Prevention.* (2013).

95. Filippini, T. *et al.*, Dietary intake of cadmium, chromium, copper, manganese, selenium and zinc in a Northern Italy community. *J Trace Elem Med Bio.* **50**, 508 (2018).

96. Rivas, A. *et al.*, Association between dietary antioxidant quality score (DAQs) and bone mineral density in Spanish women. *Nutr Hosp.* **27**, 1886 (2012).

97. Gao, J. *et al.*, Daily selenium intake in a moderate selenium deficiency area of Suzhou, China. *Food Chem.* **126**, 1088 (2011).

98.Organization, G. W. H., Vitamin and mineral requirements in human nutrition. *Geneva World Health Organization.* (2005).

99. Ren, F. & Guo, X., Characteristics, toxicity and present situation of selenium in some countries. *Foreign Medical Sciences (Section of Medgeography).* **3**, 117-119 (2004).

100. WS/T 578.3-2017, Chinese dietary reference intakes-Part 3: Trace element.

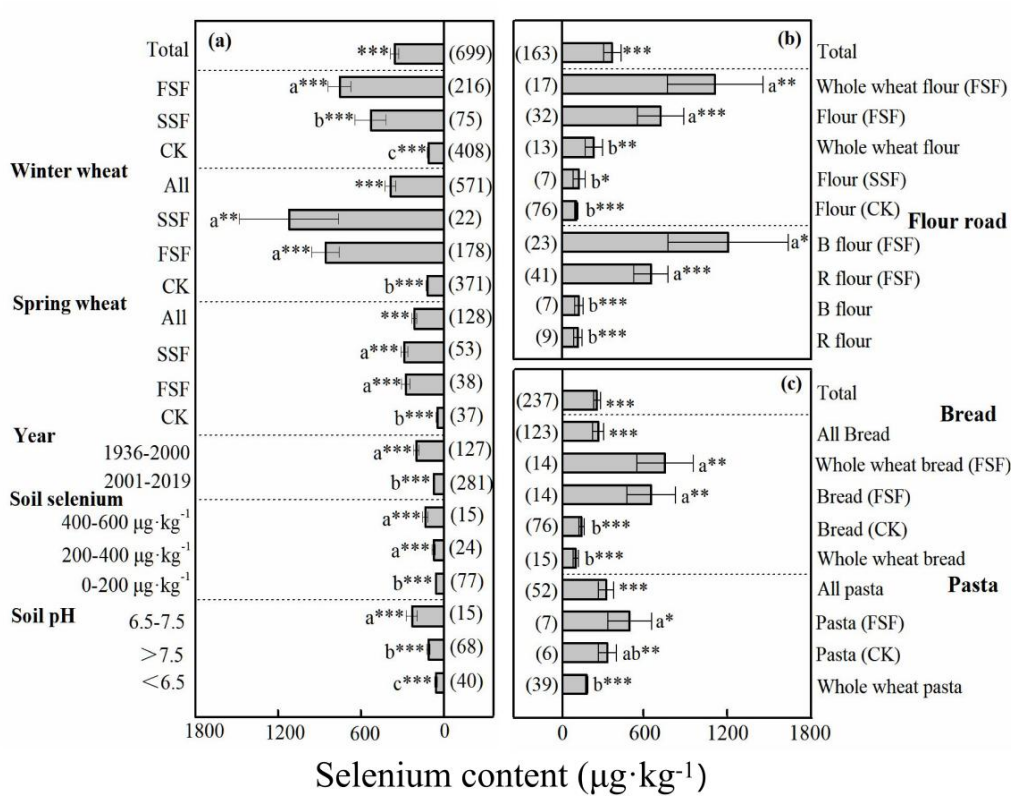

Figure 1 Comparison of Se content in wheat grain (a), flour (b) and food (c)

Note: Data originated from 66 studies; FSF: foliar Se fertilizer treatment, SSF: Soil Se fertilizer treatment; CK: unfortified Se treatment; The year is based on the harvest year of wheat; Data are presented as mean ± 95% CIs, with n in parentheses. Asterisks indicate significant differences (*$p < 0.05$, **$p < 0.01$, and ***$p < 0.001$); Different letters indicate significant differences between mean effect size for groups within each category.

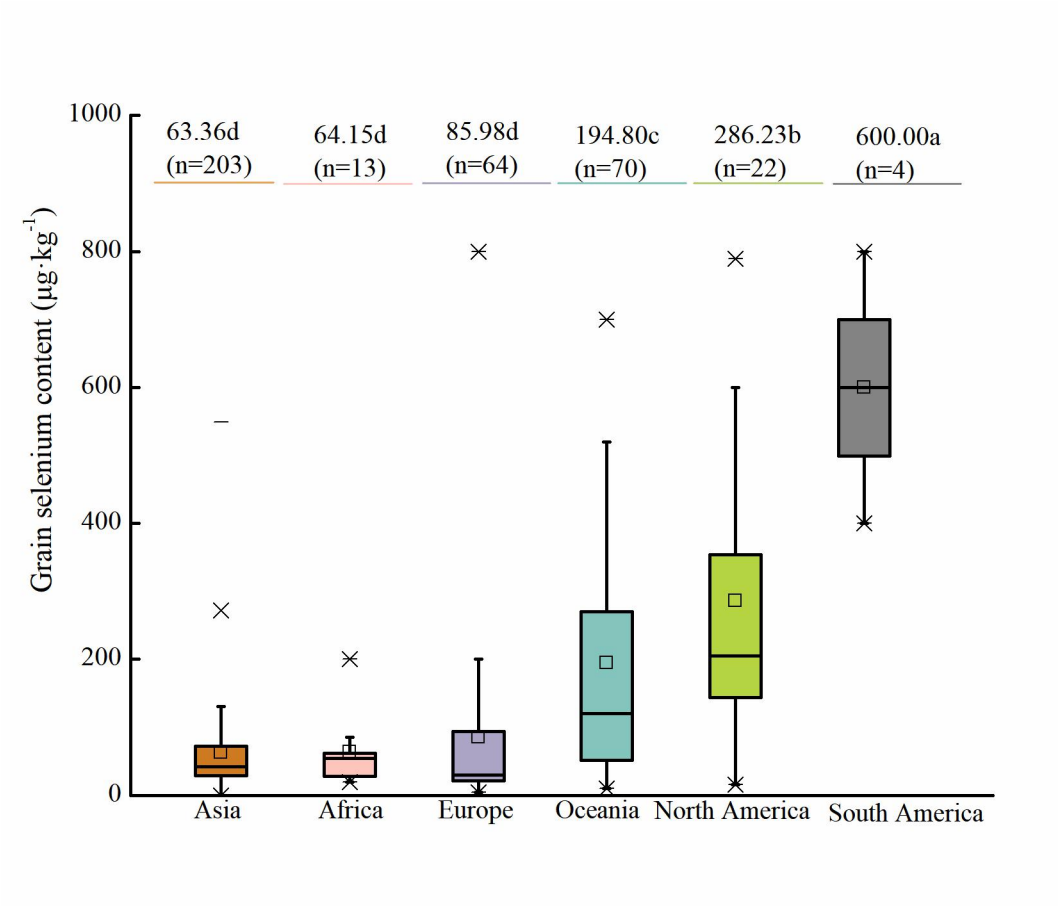

Figure 2 Selenium content of wheat among different continents

Note: Data originated from 42 studies; The letters a, b, c and d indicate a significant difference at the level of $P < 0.05$; n is the total number of samples.

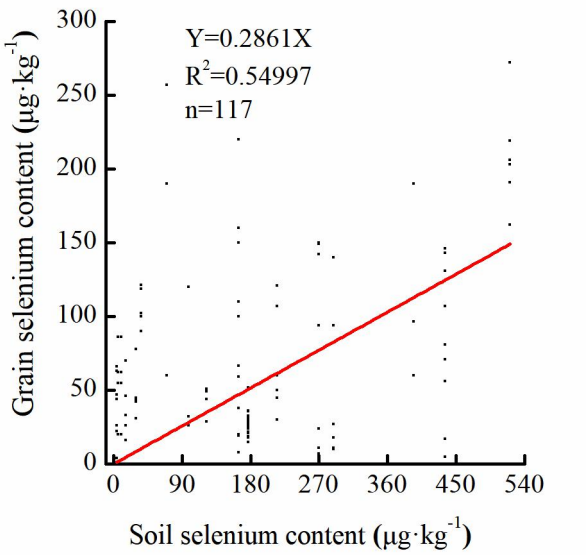

Figure 3 Relationship between soil selenium content and grain selenium content

Note: Data originated from 21 studies; n is the total number of samples.

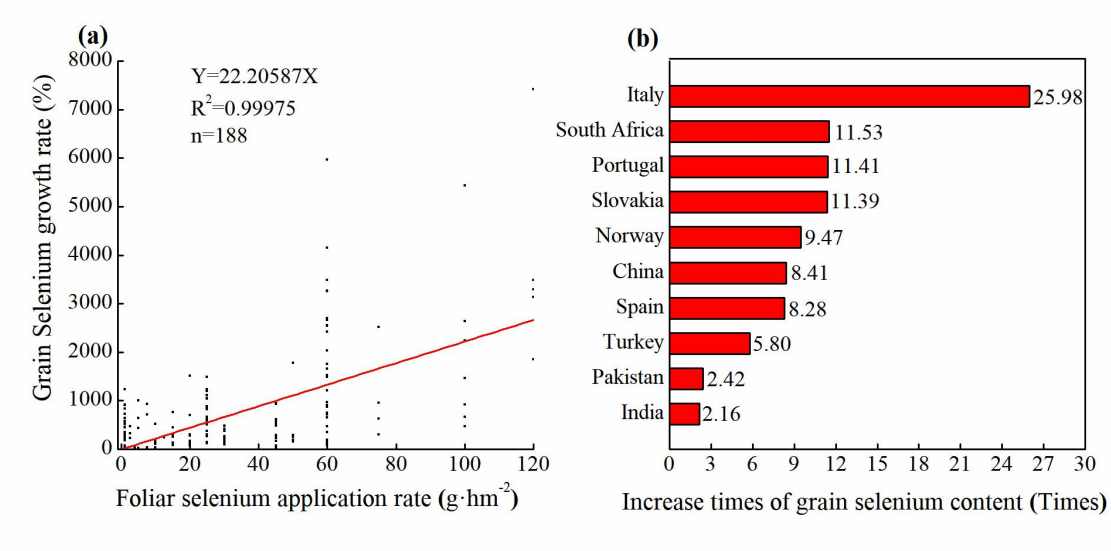

Figure 4 Relationship between foliar fertilization application rate and grain selenium content (a) and increase times of grain selenium content after fortification in different countries (b)

Note: (a) Data originated from 21 studies; Selenium was added in the form of Na_2SO_3 solution; n is the total number of samples; (b) Data originated from 42 studies.

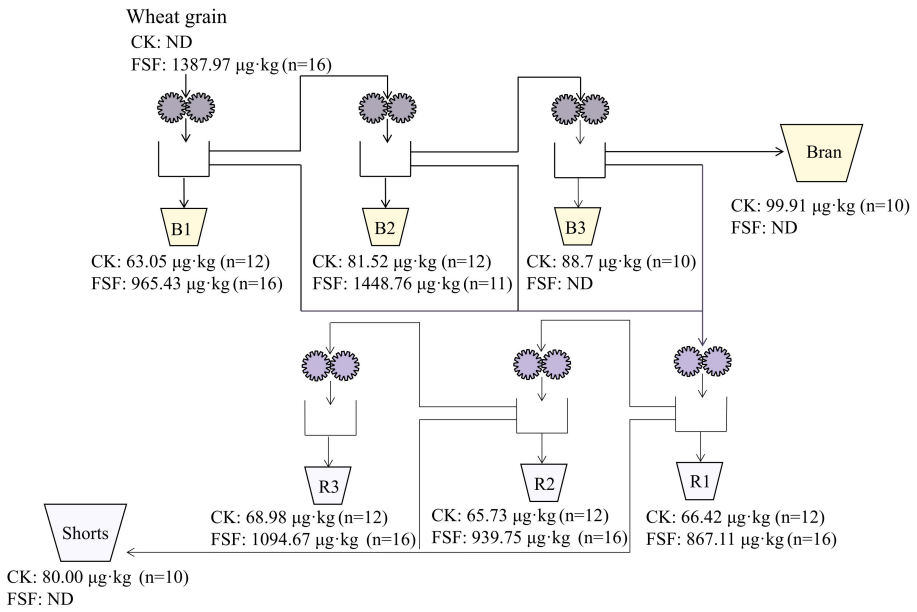

Figure 5 Schematic diagram of Selenium content in the flour road

Note: Data originated from 2 studies; B1, B2 and B3 refer to three Broken [B] milling parts; R1, R2 and R3 refer to three Reduced [R] milling parts; FSF: foliar Se fertilizer treatment, CK: unfortified Se treatment, ND: relevant information is not mentioned in the literature; The letters a, b, c and d indicate a significant difference at the level of $P < 0.05$; n is the total number of samples.

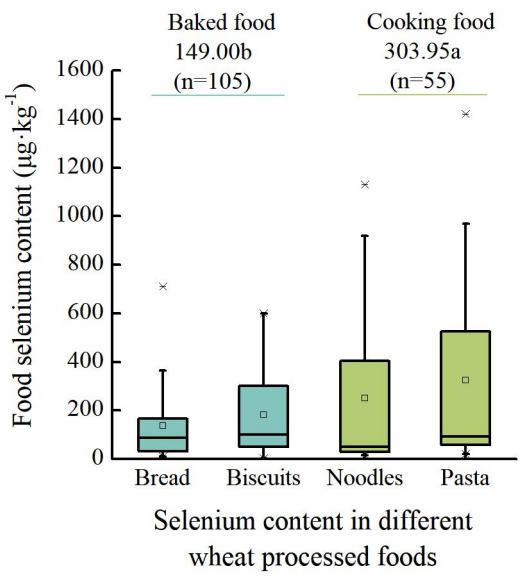

Figure 6 Selenium content in different wheat derived foods

Note: Data originated from 26 studies; The letters a and b indicate a significant difference at the level of $P < 0.05$; n is the total number of samples.

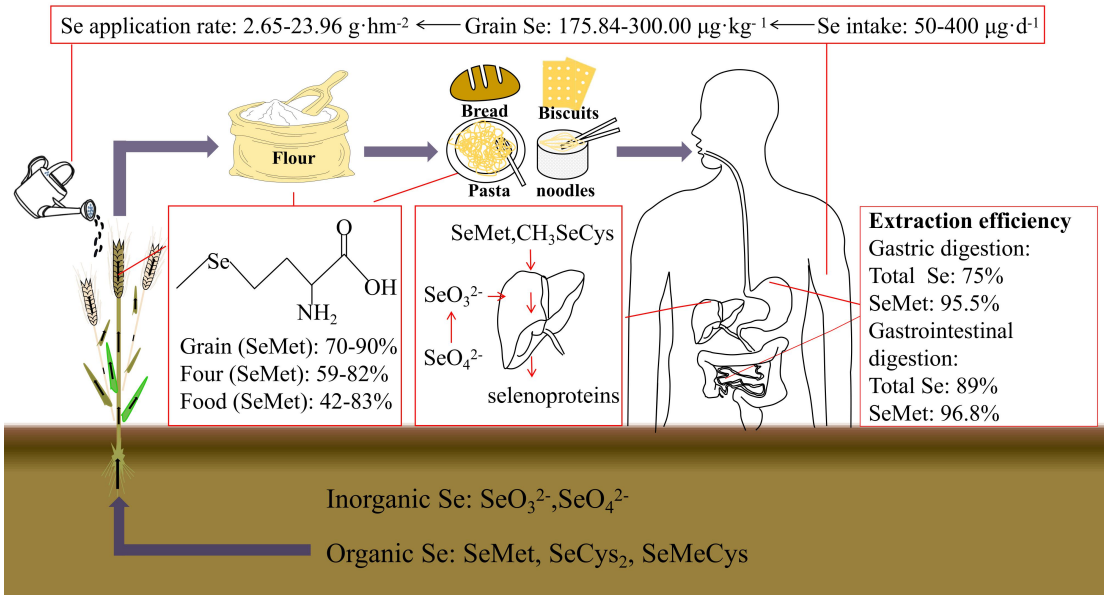

Figure 7 The change of selenium from grain to human body and the appropriate level of selenium fortification