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Selenium in selected samples of infant formulas and milk commercialized in Belgium and Brazil: Total content, speciation and estimated intake

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ABSTRACT

Total selenium (Se) and Se species concentrations were determined in 50 infant formulas and milk samples commercialized in Brazil and Belgium. Infant formula categories were starter, follow-up, specialized and plant-based (soy and rice), while milk samples included whole, skimmed, semi-skimmed and plant-based products. Total Se content was determined by Inductively Coupled Plasma Mass Spectrometry (ICP-MS), after microwave digestion. An enzymatic extraction method was applied to evaluate the Se species, mostly selenomethionine (SeMet), Se(IV) and Se(VI), through High Performance Liquid Chromatography coupled to ICP-MS (LC-ICP-MS). Starters and follow-up samples presented the highest total Se concentrations and values up to 30 μg/kg were observed in the reconstituted product. The lowest level (below the LOQ = 10 μg/kg) was verified in an anti-regurgitation specialized formula. The relative agreement between the measured total Se and the Se content declared on the label varied from 55 % to 317 %. Concentrations in infant formulas were not markedly different from concentrations in milk except for rice and oat milk samples that showed values below the LOQ. SeMet was the main species found in milks, while in infant formulas the species concentrations varied according to the product. The daily intake (DI) of Se via infant formula consumption was calculated and compared with the Adequate Intake (AI) value and the Dietary Reference Intake (DRI) established by the EFSA NDA Panel and ANVISA, respectively. Estimated maximum intakes of total Se obtained for reconstituted infant formula were 40.6 mg/day, corresponding to 400 % and 202 % of the DRI and AI, respectively.

1. Introduction

Selenium (Se) is a mineral that is necessary for human health. It is an antioxidant that has been linked to the prevention of some types of cancer and other disorders (Jin et al., 2020; Delgado et al., 2019; Thiry et al., 2012). Further, some authors highlighted the possible benefits of Se by improving behavioral and biochemical functions and chelating the toxic effects produced by the accumulation of aluminum in the brain (Lakshmi, Sudhakar & Prakash, 2015), which is particularly important in the first years of life since infant formula and baby foods are relevant sources of aluminium in the children's diet (Paiva et al., 2019; Paiva et al., 2020).

In many regions of the world, the content of Se in the diet is estimated to be insufficient and its deficiency may adversely affect health (Navarro-Alarcon and Lopez-Martinez, 2000; Pedrero and Madrid, 2009). Low Se consumption decreased glutathione peroxidase activity and plasma thyroid hormone concentrations in children with phenylketonuria who were given a low-protein diet (van Bakel et al., 2000). Fairweather-Tait et al. (2011) detailed the roles of Se in the human body, stating that selenoproteins are linked to thyroid hormone synthesis, thyroid gland activity, as well as protection (selenoproteins' redox-protective properties may be especially important in the thyroid gland). Selenoproteins, such as SelW (Selenoprotein W), SelN (Selenoprotein N), SelT (Selenoprotein T) and the 15 kDa selenoprotein have been recently suggested to be members of an unique redox protein family that is strongly associated to Ca^{2+} release (Jin et al., 2020). Se

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deficiency has been shown to influence both the cell-mediated and humoral components of the immune response in both experimental and farm animals (Hoffmann & Berry, 2008; Arthur et al., 2003). Some evidence suggests that when Se intakes are inadequate, Se supplementation can improve immunological responses in humans (Hoffmann & Berry, 2008).

Clinical disorders are also linked to severe Se deficiency. Keshan disease, for instance, is an endemic cardiomyopathy that affects primarily children and young women and is more prevalent in China's population groups with low Se consumption (Beck, 2001; Loscalzo, 2014). Se deficiency is also related to the disease of Kashin-Beck, which is a chronic degenerative osteochondropathy that occurs in preadolescence or adolescence in Se-deficient areas, such as North Korea, Siberia, China and Mongolia (Yao et al., 2011).

Nevertheless, excessively high body Se levels induced by high Se can give rise to selenosis - headache, hair loss, deformation and loss of nails, skin rash, odorous (garlic) breath and skin, severe tooth decay and discolouration, as well as numbness, paralysis, and hemiplegia are some of the symptoms. In a recent study, Amorós et al. (2018) assessed the relationship between maternal Se concentrations and child neuropsychological development finding that fetuses whose mothers had elevated Se concentrations in their serum (above 86 μg/L) could be vulnerable to Se neurotoxicity. EFSA accepts an upper limit of 45 μg/day (0 to 6 months) and 60 μg/day in infants (>6 months) and young children (EFSA, 2014; AFSSA, 2001; IOM, 2000). High Se intake can also be related to the drinking water. Rosenfeld & Beath (1964) reported a case in which a family was exposed for about 3 months to water containing 9 mg of Se per litre and suffered from loss of hair, weakened nails and mental symptoms. Epidemiological studies conducted in populations living in high Se soil content areas have suggested that chronic exposure to high Se could lead to neurotoxicity during early development (Vinceti et al., 2014).

The Food and Agriculture Organization of the United Nations (FAO) and World Health Organization (WHO) recommends intake of Se by children as a function of their age: 6 μg/day (0–6 months), 10 μg/day (7–11 months), 17 μg/day (1–3 years) and 22 μg/day (4–6 years) (CAC, 2007). The Brazilian regulation (ANVISA, 2005) uses these recommendations to establish Dietary Reference Intakes (DRI) for Se whilst the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) (EFSA, 2009) recommends Adequate Intake (AI) values in European countries of 12 μg/day (0–6 months), 15 μg/day (7–11 months), 15 μg/day (1–3 years) and 20 μg/day (4–6 years). Se supplementation in infant food is an important strategy to avoid its deficiency in infants. The Scientific Committee for Food (SCF) adopted a Tolerable Upper Intake Level (UL) of 60 μg/day for infants and young children (1–3 years; SCF, 2000).

Both the European Commission Directive 2006/141/EC of December 22nd of 2006 on infant formula and follow-on formula, supplemented by regulation commission delegated EC 2016/127 (European Commission, 2006), and the Brazilian regulation RDC n. 42 of September 19th of 2011 (ANVISA, 2011) authorize the infant formula fortification with inorganic forms of Se (selenite and selenate).

The World Health Organization (WHO) has made recommendations regarding daily mineral intake for infants and young children, but no minimum level was proposed (WHO, 2009). The same occurs for the Brazilian regulation which uses the DRIs according to the age infants group (ANVISA, 2005). DRI values have been established to aid in dietary planning and to assess whether the intake of a particular nutrient meets the requirements of individuals or populations. On the other hand, the UL is defined as the maximum level of total chronic intake of a nutrient from all sources judged to be unlikely to pose a risk of adverse health effects in humans. Following a request from the European Commission, the Scientific Committee on Food (SCF), which was the predecessor of EFSA, started off in the year 2000 with giving scientific advice in relation to ULs for vitamins and minerals (EFSA, 2014).

In a report published by the Codex Committee on Nutrition and Food for Special Dietary Uses in 1998, Se was first recommended as one of the essential nutrients in infant formula, with a maximum concentration of 7 μg/100 kcal. However, no minimum concentration was proposed by the Codex Alimentarius Commission (CAC). In 2005, an international expert group suggested that infant formula prepared ready for consumption should contain Se at the minimum and guidance upper levels of 1 and 9 μg/100 kcal, respectively. In 2019, the CODEX Alimentarium established 2 μg/100 kcal as a minimum Se level and 9 μg/100 kcal as the GUL (guidance upper level) for follow-up infant formulas (CAC, 2019). Based on the recommended intakes rates of infant formula and the available toxicity data, the Se content in infant formula is legislated in Brazil and Belgium at the same Se limits of 1–9 μg/100 kcal (ANVISA, 2011, Sluis et al, 1992), following the recommendations of the Codex Alimentarius (CAC, 2016).

In order to evaluate total Se concentration and Se species in food samples, including infant formula and baby foods, microwave-assisted digestion is the most commonly used sample preparation method (Matos-Reyes et al., 2010), followed by analysis of the digest using high temperature atomization techniques such as electrothermal atomic absorption spectrometry (ETAAS) (Tsukada & Hasegawa, 2002; de Gregori, Pinochet, Fuentes, & Potin-Gautier, 2001), inductively coupled plasma optical emission spectrometry (ICP-OES) (Nascimento et al., 2018) and inductively coupled plasma mass spectrometry (ICP-MS) (Cubadda, Raggi, Testoni, & Zanasi, 2002).

Since Se species are found in food at trace and ultra-trace levels, determining these analytes requires a very sensitive and precise analytical approach (Orecchio et al., 2014). To determine Se occurrence forms, i.e. its speciation, liquid chromatography is usually coupled to ICP-MS and this technique is applied on the samples after enzymatic digestion releasing selenoaminoacids from selenoproteins (Ling et al., 2017; Batista et al., 2011; Bierla et al., 2008). Two oxyanions, selenite ($SeO3^{2-}$ or Se(IV)) and selenate ($SeO4^{2-}$ or Se(VI)), as well as some organic species, selenomethionine (SeMet), selenocysteine (SeCys), and its methylated version, methylselenocysteine (MeSeCys), are the most well-known Se species. SeMet and SeCys are sulphur aminoacid analogues of methionine (Met) and cysteine (Cys), with a Se atom replacing the S (sulphur) atom (Johansson, Gafvelin, & Arner, 2005).

To the best of our knowledge, no data are available in Brazil and Belgium regarding Se speciation in commercialized infant formulas. A recent study reported by Almeida et al. (2022) quantified micromineral and trace mineral contents, including Se, in infant formulas commercialized in Brazil. The group found that total Se was 20 % above label values in all the infant formula brands. When considering the individual mineral daily intake, it was noted that five infant formulas exceed the tolerable limit of 45 μg/day (0–6 months) and 60 μg/day (7–12 months). Although the recent work is cited in order to compare total Se and daily intake findings, the current study approaches further information related to infant formulas speciation in order to quantify Se species and verify Se sources supplementation, when it occurs.

Therefore, motivated by the importance of maintaining an adequate Se intake, in particular for infants and young children, the current study aims to: *i*) evaluate the total Se concentration in infant formulas and milk samples commercialized in Brazil and Belgium by using a microwave digestion method followed by ICP-MS analysis; *ii*) quantify the main Se species, including selenite (SeIV), selenate (SeVI) and seleno-L-methionine (SeMet), in the samples by using LC-ICP-MS; *iii*) compare the obtained results for infant formula with information declared on the labels; and *iv*) estimate the Se daily intake though infant formula consumption and compare with reference levels (AI and DRI).

2. Materials and methods

2.1. Materials and reagents

The water utilized in this work was either double-distilled water (H_2Obidi, for ICP-MS total Se determination) or ultra-pure water obtained by purification of distilled water with the Milli-Q Gradient A10

system in combination with an Elix 3 pre-system (Millipore S.A., Billerica, USA) (H_2O mQ, for Se species determination with LC-ICP-MS). Carlo Erba supplied nitric acid (HNO_3) (Suprapur, SpA 67–69 %) (France), hydrogen peroxide (H_2O_2, 30 %) was from Merck (Germany), citric acid from Chromasolv Plus (Germany), Tris–HCl, protease XIV and lipase from Sigma-Aldrich (Belgium), and methanol from VWR (HPLC grade, Belgium).

The following reagents were used to prepare stock solutions of the different Se species, with an initial concentration of 1000 mg/L: seleno-L-methionine ≥ 98 % (SeMet), selenocysteine (SeCys) 95 %, sodium selenite (SeIV) p.a., and sodium selenate (SeVI) 99 % (Sigma-Aldrich, Belgium), and Se-methylseleno-L-cysteine 98 % (MeSeCys) (Acros, Thermo Fisher Scientific, Belgium). Stock solutions were stored at −20 °C to avoid oxidation or decomposition. Daily, appropriate dilutions were used in order to prepare a 250 mg/L multispecies stock solution. The multispecies stock solution was used to prepare final calibration standards of 0, 2, 5, 20, and 50 μg/L on a daily basis. To generate tuning solutions for ICP-MS (Varian 820, Australia), a diluted multi-elemental Varian tuning solution (5 μg/L) (Spectropure, USA) was employed in 4 % (v/v) nitric acid.

2.2. Samples

Representative samples of different types of infant formulas samples were collected in Brazil and Belgium. In the cities of Campinas, SP, Brazil, and Brussels, Belgium, 35 samples of infant formula and milk were obtained from various grocery stores and pharmacies. Among the infant formula samples, 23 were from the Brazilian and 12 from the Belgian market. The infant formulas (n = 35) were classified into five different categories stated by the *Codex Alimentarius* (CAC, 2016): standard newborns or starters (individuals from 0 to 6 months) (n = 8); follow-up standard infant formula (individuals from 6 to 12 months and from 12 to 36 months) (n = 11); starter and follow-up specialized infant formula (individuals from 0 to 6 months, 6 to 12 months, and 12 to 36 months) (n = 9); soy-based formula (n = 5); and rice-based formula (n = 2). The specialized formula sampled were: extended hydrolyzed protein, hypoallergenic, anti-regurgitation, partially hydrolyzed protein, amino acid-based hypoallergenic, and fish oil added. The milk samples (n = 15) were purchased in different Belgium supermarkets and included cow's milk (such as whole, semi-skimmed and skimmed, ultra high temperature processed) and plant-based 'milk', such as soy, rice, oat, and almond milk.

2.3. Determination of total Se

Digestion of Se was based on the AOAC Official Method 2015.06 (Pacquette et al., 2018). A sample of 1 g of reconstituted infant formula (2.5 g powder dissolved in 20 mL of H_2Obidi) or 1 g of milk was placed and weighted into a digestion tube, where 5 mL of purified HNO_3, 2 mL H_2O_2 and 0.5 mL of internal standard ($ISTD_{Ge}$) were added. After sealing the tubes, they were placed in the microwave digestor (CEM MARS Xpress, Matthews, USA) and digested using two heating ramps (power 1600 W): (a) 20 min ramp to 180 °C, hold 20 min and (b) 20 min ramp to 200 °C, hold 20 min. The tubes were opened after cooling, 20 mL of H_2Obidi was added, and the solution was transferred to a 50 mL Falcon tube. Following that, 0.5 mL methanol was added, and the solutions were diluted with H_2Obidi to a final volume of 50 mL. The Se content was determined by ICP-MS after a mass shift (*m/z* 78–94) due to a reaction in the octopole with O_2 (Agilent 8800, Agilent Technologies). Quantification was performed considering the range 0.4–16 μg/L using matrix matched Se standards. The method's limit of quantitation (LOQ) for total Se was estimated as 10 times the standard deviation of 9 process blank measurements (3 days, 3 replicates) and corresponds to 10 μg/kg Se in milk.

Se concentrations were initially obtained in μg/kg, but data were also expressed in μg/L and μg/100 kcal; therefore, the discussion section presents both units in order to compare the current data with the literature. The conversions were performed based on densities values of cow, soy, and rice milks, reported in the literature. The considered density values were: 1.01 and 1.026, for cow and soy, respectively (Oguntunde & Akintoye, 1991; Cziszter et al., 2012); 1.014 and 0.98 for rice and coconut milks, respectively (Tansakul & Chaisawang, 2006; USDA). The energy content information was obtained from the infant formula label in order to express the results in μg/100 kcal.

2.4. Se speciation

2.4.1. Extraction

Se species extraction was carried out in Tris–HCl buffer 30 mM (pH 7.5) containing 4 mg/L protease and 2 mg/L lipase using a developed and validated method, in duplicate. Approximately 1 g of reconstituted formula or 1 g of milk was extracted with 4 mL of Tris-HCl solution for one hour at 37 °C followed by the application of an ultrasonic probe for 2 min per sample (Vibra Cell, Bioblock Scientific, Illkirch, France). After that, the samples were filtrated by a molecular filter (Amicon Ultra) of 10 kDa by centrifugation (15 min, 7500g). This process was repeated two times. Finally, 2.5 mL of each filtrate was transferred to a 15 mL Falcon tube and diluted with the mobile phase solution (see section 2.4.2) to 10 mL. This mixture was transferred to a vial for measurement.

2.4.2. Se species identification and quantification

An LC-ICP-MS was used to perform the Se speciation investigations (LC system: delivery module Prostar solvent; ICP-MS: Varian 820; VARIAN, Australia). The Se species were separated using an anion exchange column (PRP-X 100, Hamilton) with a mobile phase containing 10 mM citric acid and 2 % (v/v) methanol at pH 5. The injection volume was 60 μL, and complete elution takes 10 min at a flow rate of 1.6 10^{-2} μL/s (Table 1). The peak area was quantified using the ICP-MS chromatographic software (GALAXY). Individual retention times were matched with individual standards of corresponding Se species to identify Se species. The ^{78}Se isotope was measured with H_2 as reaction gas. SeMet was quantified by standard addition of a SeMet standard solution (1–10 μg/L) in the extracts. For quantification of SeIV and SeVI, the slope of the SeMet calibration was used. The method LOQ for SeMet, SeIV, and SeVI is 3.0 μg/L in (reconstituted) milk, calculated as 10 times the standard deviation of blank data.

2.5. Method validation

Relevant certified reference materials (CRM) NIST 1849a (infant/adult nutritional formula, certified value 0.812 ± 0.029 mg/kg for total Se) and SELM-1 (Selenium enriched yeast, NRC, Canada; certified values 2031 ± 70 mg/kg for total Se and 3190 ± 260 mg/kg for SeMet) were used to assess the trueness and precision of the method. SELM-1 was

Table 1
The LC-ICP-MS system's parameters.

ICP-MS apparatus: VARIAN 820
Forward power: 1.45 kW
Gas flow (nebilizer): 0.017 L/s
Cool gas (plasma gas): 0.3 L/s
Auxiliary gas: 0.03 L/s
Sheath gas: 0.003 L/s
Gas of reaction: H_2 1.5 L/s
Sample introduction: micromist low flow nebulizer
Monitored mass: 78
HPLC system:
HPLC-pumps: PROSTAR solvent delivery module
Column: Hamilton PRP-X100. 10 μm diam particles. 0.0041 m i.d × 0.25 m length
Column oven: Eppendorf Column heather (303 K)
Isocratic flow with 10 mmol/L citric pH 5;
Flow: 1.6 10^{-2} μL/s
Injected volume: 60 μL

thereby only used for the validation of SeMet analyses (together with spiked food supplement samples), as it is the only CRM in which SeMet is certified. Together with the analysis of spiked nutritional formula samples, this resulted in an extended measurement uncertainty (U, k = 2) of 13 % for total Se analysis and 19 % for SeMet analysis.

All Se concentrations are given on volume base in milk or reconstituted infant formula samples.

The means obtained for each batch of the same brand, and between different brands, were compared by variance analysis (ANOVA) and Tukey's test ($p < 0.05$).

2.6. Daily intake estimated from the consumption of infant formulas

The daily intake of minerals depends on both concentration of the elements in food matrix and daily food consumption. Therefore, the following equation was applied in order to estimate whether Se concentrations in infant formula description are adequate: EDI = Cm × Cd (1); where EDI represents the estimated daily intake of Se, expressed as Se mg per day; Cm is the average Se concentration of infant formula description expressed as mg/100 g of formula powder; Cd is the recommended daily consumption amount stated on the label of each infant formula (suggested amount to be consumed expressed in grams per day). The approximate consumption per day is described in Supplementary Table 1. These estimated daily intakes were compared to the values of dietary reference intake (DRI) and the adequate intakes (AIs) recommended by ANVISA (2005),and the EFSA (2014).

3. Results and discussion

3.1. Total Se content and Se species in infant formula

The Se contents indicated on the labels of the analyzed products as well as the concentrations of total Se and Se species [SeMet, Se(IV), and Se(VI)] determined in the samples are described in Table 2, which presents the results separately for Belgian (BE) and Brazilian infant formulas (BR).

The Se contents indicated on the labels are similar for Belgian (range 13–39 μg/L) and Brazilian samples (6.5–32 μg/L). The highest Se levels in Belgian infant formula were indicated for the regular ones (brand A starter 39 μg/L and brand A follow-up 34 μg/L) and the same concentration range is observed for Brazilian samples (brand E follow-up with 32 μg/L). Among the specialized and plant-based products, such as rice and soy, lower values are indicated for both Belgian and Brazilian samples: brand E (BE) 14 μg/L, brand F (BE) 13.3 μg/L, brand A (BR) 6.5 μg/L and brand E (BR) 9 μg/L, respectively.

Total Se concentrations obtained by microwave digestion also indicated the highest levels for starters and follow-up infant formulas. For Belgian samples, 30.6 and 25.9 μg/L were observed for starter and follow-up both from brand A, whilst for the Brazilian ones 28.1 and 26.3 μg/L were obtained for starter brand B and follow-up brand C, respectively. The lowest values were found for brand G (BE) soy-based and brand A (BR) specialized: 10.6 and < 10 μg/L, respectively.

At the Children's Hospital of Wisconsin, a protocol was designed to fortify skimmed breast milk, containing 7 μg/L of Se, with a high-MCT (medium chain triglycerides) liquid formula (containing 18.8 μg/L of Se) to reach concentrations of 15.4 μg/L of Se, which allowed children with chylothorax disease a continued feeding on breast milk (Clark, Froh, & Polzin, 2019). The cited concentration is comparable to the findings present in this study, with values of 15.3, 16.1 and 16.3 μg/L were found for BR3, BR13 and BR18, follow-up, starter and soy infant formulas, respectively. Selenium levels in breast milk depend on maternal Se nutritional status often described as glutathione peroxidase 3 (GPx3) activity and selenoprotein P1 (SEPP1) concentration in plasma. Ideally, the AI for infants 0–6 months of age would be based on the average concentration of Se in milk from lactating women with an optimal dietary Se intake, or a level that is not lower than the recommended nutrient intake (RNI) but not more than the UL for lactating women (Xia et al., 2010). Based on milk Se concentrations of mothers with optimal daily Se intake, the adequate Se intake value and a safe range for Chinese infants 0–3 months of age were calculated as 15.29 and 8–35 μg/day of Se, respectively, in a recent Chinese assessment (Han et al., 2019). Worldwide, the variation in Se concentrations in human milk is wide, but median Se concentrations are 15 μg/L in mature milk (1–3 months) and 17 μg/L at late lactation (>5 months) (Dorea, 2002). Concerning the reported values for Se in human milk, the current study presents similar values varying from 10.9 to 30.6 μg/L for Belgium samples and from 12.1 to 28.1 μg/L for Brazilian infant formulas. In human breast milk, Michalke & Schramel (1998) observed four free Se chemical forms, GSeH selenium carrying glutathione reduced form (32 % of the total Se amount) > selenocystamine (SeCysA) (26 % of the total Se amount) > SeCys (27 %) > SeMet (non-detected).

Viñas and collaborators (2005) reported similar Se levels for starters, follow-up, and soy-based infant formula in the range of 4.9 – 14.1 μg/L for samples commercialized in Spain (the values were recalculated here on reconstituted base (dilution factor 9) in order to allow the comparison with the present study). Van Dael and Barclay (2006) showed Se levels in reconstituted infant formula from different countries and found total Se levels between 3.4 and 13.6 μg/L, which is also in accordance with the present study. Spanish milk-based ready-to-use infant formulas had higher levels, ranging from 18 to 50 μg/L. On the other hand, Navarro-Blasco and Avarez-Galindo (2004) measured total Se in Spanish reconstituted infant formulas and found lower values for non-adapted starting formulations ranging from 2.9 to 17.3 μg/L.

In the specialized infant formula, the values for total Se varied from 10.6 to 25.8 μg/L and from < 10 to 17.7 μg/L, for Belgian and Brazilian samples, respectively. The same profile was observed by Lopez et al. (2019), who analyzed samples obtained from local markets of San Luis City, Argentina, and found mean total Se content in specialized samples of 17.4 μg/L. According to the authors, the specialized formula present low levels of milk fat (25 %), such as skimmed milk. Martino et al. (2001) also reported a study in reconstituted infant formula based on whole milk, skimmed milk and milk whey, with total Se concentration decreasing from 17.5 to 14 μg/L and non-detected, respectively.

For Brazilian and Belgian samples, low total Se concentrations were measured in plant-based infant formula, such as rice and soy, with the lowest level of 10.6 μg/kg for brand G (BE). Van Dael and Barclay (2006) obtained even lower values for soy-based reconstituted commercialized infant formula in The Netherlands, with a mean value of 3.4 μg/kg.

Total Se concentrations reported on the labels and measured values were compared with the aim of verifying if the label statement content is reliable with regard to the Se concentration in infant formula samples. According to Table 2, a mean recovery of 121 % with a range of 62–137 % for Belgian samples, and a mean recovery of 143 %, with a range of 57–316 % for Brazilian samples were observed. Most of these differences can be explained by analytical uncertainties. Spanish infant formula powder samples were analyzed by Chávez-Servín et al. (2008), who presented recovery values of 64–84 % with respect to the label. This corroborates with the deviations found in our study.

Concerning the comparison between the Se guidance minimum and upper levels of 1 and 9 μg/100 kcal established by CAC (2005), all the samples values reported in Table 2 are in agreement with the recommendation once the values varied from 1.4 to 5.7 μg/100 kcal; however, higher mean values were recently found by Almeida and collaborators (2022) which reported a range between 4.0 and 9 μg/100 kcal.

Regarding the Se species, our study reported a mean value of 6.7 and 12.5 μg/L for SeMet in Belgian and Brazilian infant formula, with a range of < 3 to 14 μg/L and 4 to 45 μg/L, respectively (Table 2). Lopez et al. (2019) reported an average value of 8 μg/L of SeMet in reconstituted infant formula (range: 7.5 to 8.3 μg/L), which is in agreement to the levels found in the present work. Concerning Se(IV), Viñas et al. (2005) obtained concentrations in the range of 8.5 to 13.5 μg/L in reconstituted infant formulas available in Spanish markets, whilst in the

Table 2
Total Se and Se species [SeMet, Se(IV) and Se(VI)] concentrations (mean ± standard deviations) in infant formula.

Brand	Sample description	Se label content (μg/L)	Se total measured (μg/L)	Relative agreement (%)	Se total measured (μg/kg)	Se total measured (μg/100 kcal)	SeMet (μg/L)	Se IV (μg/L)	Se VI (μg/L)	Label
	Belgian (BE)									
A	*BE1* Starter	39.0	30.3 ± 0.2[a]	77.7	30.6 ± 0.2[a]	1.4 ± 0.2[a]	7.0 ± 7.0	<LOQ	37.0 ± 3.0	Sodium selenate
	BE2 Follow-up	34.0	25.7 ± 0.7[b]	75.6	25.9 ± 0.7[b]	2.1 ± 0.7[b]	4.0 ± 2.0	<LOQ	19.0 ± 1.0	Sodium selenate
	BE3 Extended hydrolyzed protein	23.0	14.2 ± 0.6[c]	61.7	14.4 ± 0.6[c]	2.8 ± 0.6[c]	14.0 ± 4.0	<LOQ	<LOQ	Not found
B	*BE4* Starter	13.0	10.8 ± 0.8[d]	83.1	10.9 ± 0.8[d]	5.7 ± 0.8[d]	<LOQ	<LOQ	<LOQ	Sodium selenate
	BE5 Follow-up	15.0	12.0 ± 0.8[d]	80.0	12.1 ± 0.8[d]	2.3 ± 0.8[d]	5.0 ± 15	<LOQ	6.2 ± 3.0	Sodium selenate
C	*BE6* Follow-up	16.0	20.1 ± 0.8[c]	126	20.3 ± 0.8[c]	2.1 ± 0.8[c]	4.0 ± 4.0	9.0 ± 0.7	<LOQ	Sodium selenite
D	*BE7* Hypoallergenic	15.0	17.7 ± 1.0[c]	118	17.9 ± 1.0[c]	2.1 ± 1.0[c]	9.0 ± 7.0	10.0 ± 1.0	<LOQ	Not found
	BE8 Hypoallergenic	24.0	25.8 ± 1.2[b]	107	26.1 ± 1.2[b]	2.1 ± 1.2[b]	9.0 ± 5.0	22.0 ± 3.0	3.0 ± 3.0	Not found
E	*BE9* Anti-regurgitation	14.0	11.7 ± 0.9[d]	83.6	11.8 ± 0.9[d]	5.7 ± 0.9[d]	7.0 ± 10	<LOQ	<LOQ	Sodium selenite
F	*BE10* Rice	15.0	17.7 ± 0.4[c]	118	17.9 ± 0.4[c]	2.2 ± 0.4[c]	8.0 ± 5.0	17.0 ± 1.0	3.0 ± 8.0	Sodium selenite
	BE11 Rice	13.3	17.8 ± 2.2[c]	137	18.1 ± 2.2[c]	2.2 ± 2.2[c]	8.0 ± 7.0	15.0 ± 2.0	3.0 ± 12	Sodium selenite
G	*BE12* Soy	Not found	10.6 ± 0.7[d]	77.7	10.9 ± 0.7[d]	Not found	4.0 ± 1.0	<LOQ	18.0 ± 2.0	Sodium selenate
	Brazilian (BR)									
A	*BR1* Starter	17.0	17.6 ± 0.1[c]	103	17.8 ± 0.1[c]	2.7 ± 0.1[c]	35.0 ± 6.0	<LOQ	3.0 ± 9.0	Sodium selenite
	BR2 Starter	17.0	17.4 ± 0.6[c]	102	17.6 ± 0.6[c]	2.2 ± 0.6[c]	6.0 ± 1.0	<LOQ	3.0 ± 6.0	Sodium selenite
	BR3 Follow up	15.7	16.2 ± 0.1[c]	103	16.3 ± 0.1[c]	2.8 ± 0.1[c]	28.0 ± 2.0	4.0 ± 5.0	3.0 ± 0.3	Sodium selenite
	BR4 Anti-Regurgitation	6.5	<LOQ	81.5	<LOQ	<LOQ	7.0 ± 0.4	<LOQ	3.0 ± 17	Sodium selenite
	BR5 Partially hydrolyzed protein	16.0	12.2 ± 0.7[d]	76.3	12.3 ± 0.7[d]	3.1 ± 0.7[d]	4.0 ± 7.0	6.0 ± 3.0	<LOQ	Sodium selenite
	BR6 Amino acid-based hypoallergenic	12.4	14.0 ± 0.4[c,d]	113	14.1 ± 0.4[c,d]	1.8 ± 0.4[c,d]	4.0 ± 14	19.0 ± 0.1	3.0 ± 6.0	Sodium selenite
	BR7 Soy	16.0	14.2 ± 0.4[c,d]	88.8	14.5 ± 0.4[c,d]	1.9 ± 0.4[c,d]	11.0 ± 0.4	4.0 ± 5.0	3.0 ± 3.0	Sodium selenite
	BR8 Soy	30.0	17.5 ± 0.9[c]	58.3	17.9 ± 0.9[c]	1.8 ± 0.9[c]	12.0 ± 4.0	5.0 ± 3.0	<LOQ	Sodium selenite
B	*BR9* Starter	21.0	27.8 ± 1.0[b]	132	28.1 ± 1.0[b]	1.5 ± 1.0[b]	46.0 ± 22	16.0 ± 1.0	3.0 ± 4.0	Sodium selenite
	BR10 Starter	17.0	18.2 ± 0.8[c]	107	18.3 ± 0.8[c]	1.5 ± 0.8[c]	8.0 ± 12	<LOQ	3.0 ± 17	Sodium selenite
	BR11 Follow up	28.0	23.7 ± 2.5[c,b]	84.6	23.9 ± 2.5[c,b]	2.3 ± 2.5[c,b]	10.0 ± 1.0	11.0 ± 4.0	<LOQ	Sodium selenite
	BR12 Fish oil	11.3	<LOQ	62.8	<LOQ	<LOQ	8.0 ± 8.0	<LOQ	3.0 ± 6.0	Sodium selenite
C	*BR13* Starter	18.0	15.9 ± 0.9[c]	88.3	16.1 ± 0.9[c]	2.1 ± 0.9[c]	4.0 ± 5.0	3.0 ± 4.0	9.0 ± 27	Sodium selenite
	BR14 Starter	10.4	19.7 ± 0.4[c]	189	19.8 ± 0.4[c]	3.4 ± 0.4[c]	10.0 ± 21	<LOQ	9.0 ± 0.5	Sodium selenite
	BR15 Follow up	21.0	18.6 ± 0.5[c]	88.6	18.7 ± 0.5[c]	3.0 ± 0.5[c]	10.0 ± 3.0	3.0 ± 6.0	13.0 ± 4.0	Sodium selenate
	BR16 Follow up	25.0	26.1 ± 2.1[b]	104	26.3 ± 2.1[b]	2.8 ± 2.1[b]	7.0 ± 10	<LOQ	3.0 ± 5.0	Sodium selenite
	BR17 Extended hydrolyzed protein	16.0	11.9 ± 0.2[d]	74.4	12.1 ± 0.2[d]	1.8 ± 0.2[d]	10.0 ± 4.0	<LOQ	<LOQ	Sodium selenite
	BR18 Soy	13.0	14.9 ± 1.6[c,d]	114	15.3 ± 1.6[c,d]	2.3 ± 1.6[c,d]	15.0 ± 4.0	<LOQ	3.0 ± 2.0	Sodium selenite
D	*BR19* Follow up	8.0	25.4 ± 0.9[b]	317	25.6 ± 0.9[b]	3.5 ± 0.9[b]	10.0 ± 1.0	<LOQ	21.0 ± 20	Sodium selenate
E	*BR20* Follow up	32.0	18.2 ± 0.2[c]	56.9	18.4 ± 0.2[c]	2.1 ± 0.2[c]	6.0 ± 4.0	4.0 ± 10	3.0 ± 13	Sodium selenite
	BR21 Follow up	32.0	22.2 ± 1.1[b,c]	69.4	22.4 ± 1.1[b,c]	2.3 ± 1.1[b,c]				

(*continued on next page*)

Table 2 (*continued*)

Brand	Sample description	Se label content (μg/L)	Se total measured (μg/L)	Relative agreement (%)	Se total measured (μg/kg)	Se total measured (μg/100 kcal)	SeMet (μg/L)	Se IV (μg/L)	Se VI (μg/L)	Label
							6.0 ± 2.0	5.0 ± 2.0	3.0 ± 3.0	Sodium selenite
	BR22 Follow up	32.0	17.7 ± 0.6[c]	55.3	17.8 ± 0.6[c]	2.2 ± 0.6[c]	6.0 ± 2.0	4.0 ± 2.0	3.0 ± 2.0	Sodium selenite
	BR23 Soy	9.0	17.7 ± 0.9[c]	197	18.2 ± 0.9[c]	2.3 ± 0.9[c]	7.0 ± 2.0	5.0 ± 6.0	3.0 ± 2.0	Sodium selenite

Limits of quantitation (LOQ) of 10.0 μg/kg and 3.0 μg/kg for total and Se species, respectively.
[a,b,c,d]Mean values between different rows with the same letter are not significantly different at $p > 0.05$, according to Tukey's test.

current work the observed range varied from 0.3 to 22 μg/L. Regarding Se(VI), the concentrations varied from 2 to 37 μg/L among Belgian and Brazilian samples, whereas Viñas et al. (2005) could not quantify this Se species.

3.2. Total Se content and Se species in milk samples

The analysis of milk samples beyond infant formula samples aimed to obtain information about the background Se concentration in milk, in absence of direct Se supplementation as is often applied in infant formula. This information could help to reveal to what extent infant formula were indeed enriched or contained only background Se levels. It must be realized that also this background level (and its species distribution) could have been influenced by the cow's feed composition and Se supplementation, conducted in Belgium (selenite vs SeMet vs selenized yeast).

Table 3 presents the Se species [SeMet and Se(VI)] concentrations in 15 different Belgian milk samples, including cow and plant-based milks. The results demonstrate lower levels of SeMet and Se(VI) in plant-based milk samples, and higher concentrations for cow's milk, including whole, skimmed and semi-skimmed products. Mean concentrations for SeMet ranged from 14.8 to 40.0 μg/ L for cow's milk and from not detected to 20.1 μg/L in plant-based ones. Muñiz-Naveiro et al. (2007) conduct a speciation analysis in Spanish cow's milk samples and found levels below the limits of detection (LOD) for Se(VI) (LOD = 1.7 μg/L) and SeMet (LOD = 2.9 μg/L). However, after organic cow feed Se supplementation (0.5 μg/g), a mean concentration of 8.5 μg/L for SeMet was observed while levels below the LOD were still reported for Se(VI). For the species Se(IV), all milk samples in our study were below the LOQ (3 μg/L). In contrast to infant formula, milk samples do not present total Se concentrations on the labels.

For SeMet concentrations, an average value of 19.6 μg/L was obtained in milk whilst for Se(VI) the mean concentration was 3 μg/L in the current study. For Se(IV) none of the analyzed samples were above the established LOQ.

Table 4 shows the total Se levels in milk (cow's, sheep's, and nut milk) from 13 countries for comparison purposes.

Se concentrations observed in Belgian whole cow's milk (Table 3) are comparable to those found in most countries (Table 4). However, our concentrations are lower than the levels determined in Se rich areas, such as the Amazon region in Brazil (Lemire et al., 2010) and Argentina (Lopez et al., 2019), whilst lower amounts were reported in Spain (Martino et al., 2001), Portugal (Delgado et al., 2019), Greece (Pappa et al., 2006) and Ireland (Murphy & Cashman, 2001).

In general, the lowest levels are described for plant-based samples, such as rice, soy, oat and almond milk. Pedron et al. (2016) studied essential and non-essential elements in Brazilian rice-based milks consumed by celiac population and observed a total Se content of 2 and 28 μg/L for rice- and non-rice-based milk, respectively. Delgado et al. (2019) developed a study regarding Se content in Portuguese key foods based on the comparison between food composition databases. The total Se contents in whole milk varied from 10 to 50 μg/L, which are similar to the concentrations reported in the present work. Khan and colleagues (2014) used microwave digestion followed by ICP-MS quantification to examine 64 milk samples obtained from supermarkets around South Korea and found high total mean Se concentrations of 1399 and 1425 μg/L for plain and skimmed milk, respectively.

Among milk samples (Table 4), the highest Se levels were reported in the Brazilian milks, both nut and cow's, with values of 630 and 60 μg/L respectively. The milk nut is made from Brazilian nuts, and it is generally known that the Brazilian nut (*Bertholletia excelsa*), which belongs to the Lecitidaceae family, is a Se-accumulator plant (Fordyce, 2005). Other factors that may represent differences in Se concentrations in food are the variable Se concentration in soils, which is attributed to a number of regional factors (Hoffman-Pennesi et al., 2015), as well as differences in plant cultivars (Lemire et al., 2010). Martino et al. (2001) reported a study regarding the distribution patterns of essential elements in reconstituted infant formula based on whole milk, skimmed milk and milk whey, with total Se concentration decreasing from 17.5 to 14 μg/L and non-detected, respectively. In comparison to whole milk, skimmed milk may contain lower levels of Se, since seleno-amino acids, mainly SeMet and SeCys, are bound to the protein phase (Ling et al., 2017).

Inorganic Se was not discovered in human breast milk and accounted for around 30 % of total Se in cow milk, according to Bierla et al. (2008). SeMet was the predominant Se form associated with breast milk whey, according to Al-Awadi & Srikumar (2001), whereas SeCys content was insignificant.

4. Estimated daily dietary Se intake through infant formula consumption

Fig. 1 presents the results in terms of Se intake in mg per day. An UL was considered for each infant formula description, which states a lower value of 45 μg/day only for starters, and 60 μg/day for the follow-up, specialized, rice and soy formulas description. The figure also presents the minimum Se daily intake according to the age range from (0 to 6) and (6 to 12) months and current international legislation as shown in Supplementary Table 2.

It was observed that for starters, the minimum Se intake was achieved for all the samples when the lowest level of 6 μg/day (DRI) was considered, whilst BE1, BR2, BR9, BR10 and BR13 sample did not achieved the minimum value of 15 μg/day (AI). Therefore, considering that when breastfeeding cannot be performed and infant formulas are the only food source offered to infants aged 0–6 months, and that nutritional requirements of the diet during the infant's initial phase are highest, an inadequacy of Se can negatively impact infant health.

Concerning follow-up, specialized, soy and rice infant formula, few samples were below the minimum value of 15 μg/day, BE6 and BR20; BR6 and BR17; BR7, BR8, and BE10, respectively. However, there may be no such concern, since from that period of 6 months onward, infant formula or breastfeeding intake should be complemented from other foods sources that could supply infant needs.

Considering the highest measured Se intake in the current study (40 μg/day), and the reported values in Fig. 1, no toxic effect of Se in infant

Table 3
Se content in cow's, sheep's and plant milk samples reported in other studies.

Country	Se total (μg/kg)	Se total (μg/L)	n	Type of sample	Reference
Belgium	10.0 ± 0.5	10.1 ± 0.5	–	Raw cow's milk	Shen et al. (1996)
Greece	13 ± 22	13.1 ± 22		Cow's milk	Pappa et al. (2006)
Ireland	14 ± 18	14.1 ± 18		Cow's milk	Murphy and Cashman (2001)
Japan	17.5 ± 3.6	17.6 ± 3.6	13	Cow's milk	Tamari et al. (1990)
Burundi	26.0 ± 5.5	26.2 ± 5.5	19	Cow's milk raw	Benemariya et al. (1993)
	12 ± 2	12.1 ± 2		Cow's milk processed	
Argentina	41.1 ± 0.1	41.5 ± 0.1	10	Cow's milk	Lopez et al. (2019)
	48.1 ± 0.2	48.5 ± 0.2			
Italy	48.7 ± 0.2	49.1 ± 0.2	10	Sheep's milk	
	46.5 ± 0.2	46.9 ± 0.2			
Estonia	46.0 ± 1.0	46.1 ± 1.0	10	Cow's milk	Ling et al. (2017)
Spain	12.8 ± 1.3	12.9 ± 1.3	–	Cow's milk	Martino et al. (2001)
	11.3 ± 1.9	11.4 ± 1.9	–	Sterilized milk	
Portugal	4.5 ± 2.6	4.6 ± 2.6	36	Cow's milk	Delgado et al. (2019)
Sweden	17.0 ± 0.4	17.1 ± 0.4	9	Cow's milk	Ljung et al. (2011)
Canary Island - Spain	16.5 ± 4.5	16.6 ± 4.5	8	Raw cow's milk	Rodriguez et al. (2001)
	14.9 ± 2.8	15 ± 2.8	18	Sterilized cow's milk	
Brazil	630 ± 2	636 ± 2	3	Nut milk	Lemire et al. (2010)
	60.0 ± 0.1	61 ± 0.1	5	Cow's milk	
	2.0 ± 1.0	2.0 ± 1.0	3	Rice milk	Pedron et al. (2016)
	28 ± 9	28.2 ± 9	3	Cow's milk	
USA	32 ± 27	32.1 ± 27	312	Cow's milk	Van Dael & Barclay (2006)
Australia	12 ± 22	12.1 ± 22	10	Cow's milk	
South Korea	1399 ± 5.7	1413 ± 5.7	33	Cow's plain milk	Khan et al. (2014)
	1424 ± 5.5	1438 ± 5.5	31	Cows skimmed milk	
Belgium	23.3 ± 4.7	23.5 ± 4.7	8	Whole cow's milk	Present study
	30.3 ± 1.7	30.6 ± 1.7		Skimmed milk	
	11.3 ± 1.7	11.4 ± 1.7		Semi-skimmed milk	
	12 ± 0.4	12.3 ± 0.4	2	Soy Milk	
	1.5 ± 0.9	1.5 ± 0.9	2	Oat milk	
	0.5 ± 0.1	0.5 ± 0.1	2	Rice milk	
	11.9 ± 2.4	12.0 ± 2.4	11.7	Coconut milk (with rice)	

formula is expected. In a recent study regarding macro and micro-minerals present in infant formulas commercialized in Brazil, Almeida et al. (2022) found higher values varying from of 78 to 120 μg/day which exceeds the upper limit of 60 μg/day. Therefore, monitoring Se concentrations in foods is relevant from both a regulatory and public health perspective.

Table 4
Total Se and Se species [SeMet, Se (VI)] concentrations (mean ± standard deviation) in milk samples from Belgian brands.

Brand	Milk type	Se total extracted (μg/L)	SeMet (μg/L)	Se VI (μg/L)
A	Semi skimmed milk	11 ± 2	40 ± 35	< LOQ
	Oat milk	< LOQ	6 ± 3	< LOQ
B	Semi skimmed milk	< LOQ	< LOQ	< LOQ
	Whole Milk	22 ± 3	25 ± 3	< LOQ
	Soy Milk	< LOQ	20 ± 2	3 ± 12
	Oat milk	< LOQ	15 ± 14	< LOQ
	Rice milk	< LOQ	23 ± 24	3 ± 3
C	Skimmed milk	31 ± 3	33 ± 18	< LOQ
	Whole Milk	16 ± 6	18 ± 10	< LOQ
D	Lactose free	< LOQ ± 0.5	6 ± 1	3 ± 8
E	Semi skimmed milk	14.5 ± 0.1	15 ± 3	3 ± 1
F	Soy Milk	18.9 ± 0.4	18 ± 12	3 ± 2
	Coconut milk (with rice)	12 ± 2	16 ± 4	3 ± 4
G	Skimmed milk	21 ± 0.3	20 ± 8	< LOQ
H	Rice milk	< LOQ	< LOQ	3 ± 5

Limits of quantitation (LOQ) of 10.0 μg/kg and 3.0 μg/kg for total Se and Se species, respectively.

Figure S1 (Supplementary Fig. 1) presents the estimated daily dietary Se intake (mg/day) based on an average milk consumption of 0.8 L/day for infants aged 0 to 6 months and 0.6 L/day for infants aged 7 to 12 months (Heinig et al., 1993) and the results were also calculated as a percentage of the respective AI and DRI values. Considering the maximum concentration values of total Se obtained for reconstituted infant formula, the estimated daily intake corresponded up to 400 % and 202 % of the DRI and AI, respectively.

It is important to mention that this estimate does not consider the fact that powdered infant formulas must be reconstituted with drinking water (which also contains minerals) prior to consumption.

A recent study revealed Se intake as suboptimal for breastfeeding infants in New Zealand. Estimated median infant Se intakes at 3 and 6 months were 85 % and 93 % below the AI of 12 μg/day (Jin et al., 2020). Another study using commercial infant formulas from the Spanish market to estimate newborn Se intake found that infants in their first month of life had a Se consumption of<10 μg/ day (Navarro-Blasco and Avarez-Galindo, 2004). Based on milk Se concentrations of mothers with optimal daily Se intake, the adequate Se intake value and a safe range for Chinese infants 0–3 months of age were calculated as 15.3 and 8–35 μg/day, respectively, in a recent Chinese assessment (Han et al., 2019).

Using representatively pooled samples from five different nations, including Germany, Italy, France, Spain, and the United Kingdom, a relatively low mean Se intake of 10.3 μg/day was estimated for newborns solely fed with infant formula during the first four months of life (Pandelova et al., 2012).Se presents a quite narrow gap between essential and toxic doses (Thiry et al., 2012).

In 2014, a scientific opinion on dietary reference values for Se issue by EFSA, has present a complete background related to Se intake (EFSA, 2014). According to the panel, there are no methods available that can reliably extract the totality of selenium from foods without potentially affecting the chemical structure of selenium compounds (Fairweather-Tait et al., 2010). The selenium content of grains and vegetables generally depends on the selenium content of the soil, as well as on its geochemical characteristics (Johnson et al., 2010; Mehdi et al., 2013): the uptake of selenium by plants depends on soil pH, redox potential and water content. Wheat, other grains and soya beans contain predominantly selenomethionine with smaller amounts of selenocysteine and selenate (Cubadda et al., 2010). Data on the forms of selenium in animal foods are limited, and the selenium content of foods from animal sources varies according to the diet of the animals (Mehdi et al., 2013). The main food groups contributing to selenium intake were milk and dairy products, meat and meat products, grains and grain-based products and fish and fish products. Based on this information an overview of dietary

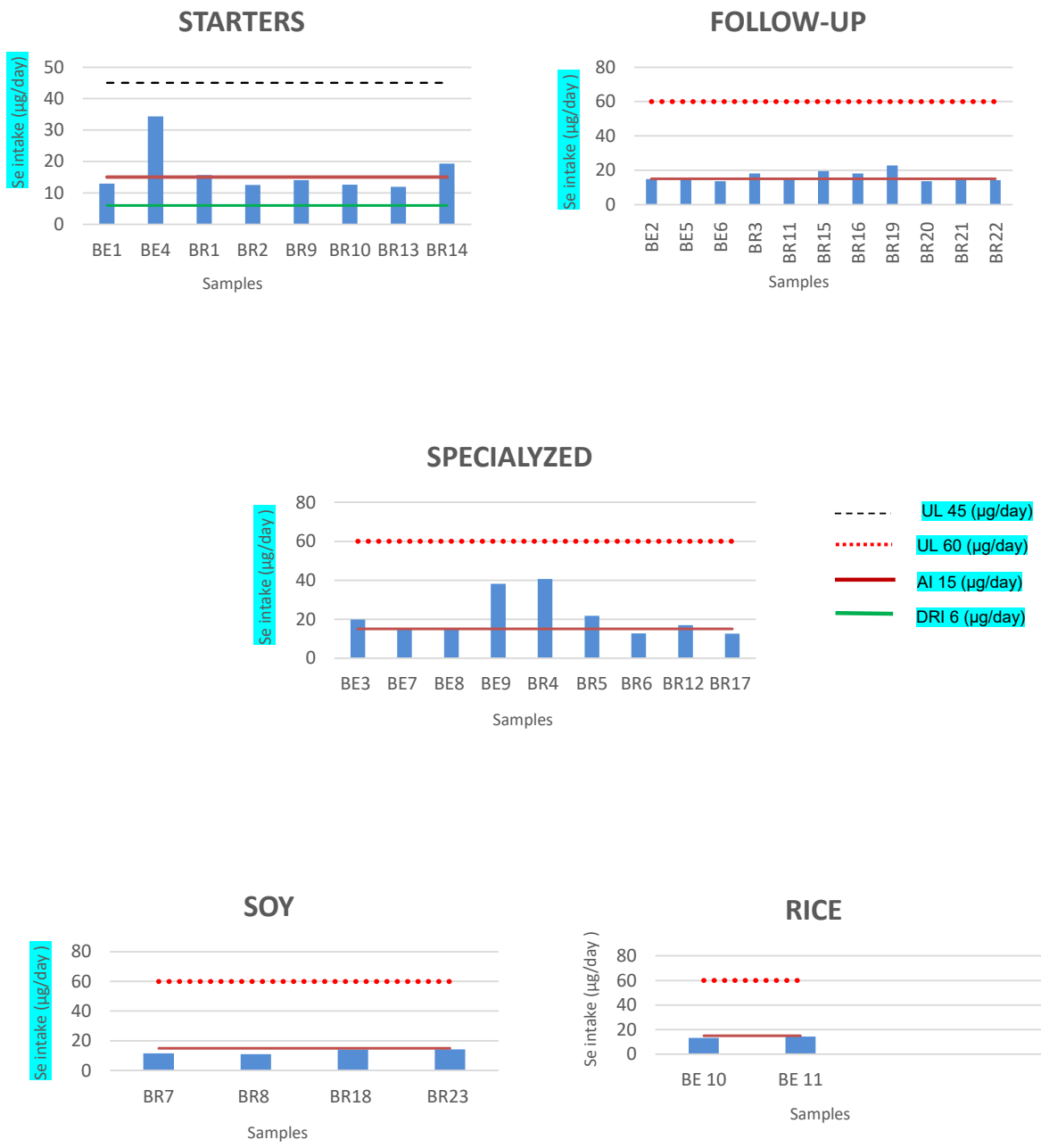

Fig. 1. Daily intake values calculated for Se of infant formula types and their adequate intake (AI), DRI (Dietary daily intake) and UL (Upper tolerable intakes) for children aged from (0 to 6) and (6 to 12) months. Upper tolerable intake values according to current international legislation are shown in Supplementary Table 2. The daily intake values of Se come from Supplementary Table 3. IFs, infant formulas; UL, upper tolerable level intakes.

reference values and recommendations for children was proposed with Se varying from 8 to 30 µg/day for children from 4 to 12 months age (WHO/FAO, 2004; Afsaa, 2001; IOM, 2000; SCF, 2000; EFSA, 2014).

Overall, the present study has achieved its aim of examining Se concentrations in infant formulas from Brazil and Belgium and milk samples to determine whether they are within relevant regulatory ranges. However, inadequacy regarding the minimum values established in the current legislation was observed mainly for starter infant formulas with some batches found to be lower than the AI.

5. Conclusions

Total Se content and the species SeMet, Se(IV) and Se(VI) concentrations were determined in samples of infant formula collected on the Belgian and Brazilian markets. Large variations were observed in total Se concentrations of infant formula which may be related to the amount of Se supplemented (in function of age group) and the natural level of the milk used (influenced by the type of formula). Compared with Se concentrations provided on the label, a mean relative agreement of 103 % between the label information and the measured Se concentration was verified.

The recommended intake was met for most starter infant formula. In follow-up formula this is not always the case, but it is not the sole source of Se for infants. Se speciation plays a role in absorption of Se; total Se values are not a perfect indicator for the nutritional status of the infant formula. Infant formula derived from plant proteins do contain less Se

and the specie used for fortification is mostly Se(IV), the least absorbed Se form. Special attention is needed for vegetable based diets as Se intake is not met by the consumption of the infant formula only. In addition, some aspects of infant formula composition should be re-evaluated and improved to meet current international guidelines, as the ideal compositional, quality, and safety requirements for infant formula must be carefully followed when the major population health effects in adulthood are associated with obesity or poor childhood nutrition.

CRediT authorship contribution statement

Esther Lima de Paiva: Writing – original draft, Writing – review & editing, Investigation. **Ann Ruttens:** Resources. **Nadia Waegeneers:** Data curation. **Gijs Du Laing:** Conceptualization. **Marcelo Antônio Morgano:** Validation. **Karlien Cheyns:** Writing – review & editing, Validation. **Adriana Pavesi Arisseto-Bragotto:** Supervision, Investigation, Conceptualization.

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.

Data availability

Data will be made available on request.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.foodres.2022.112289.

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