Aluminum bioaccessibility in infant formulas commercialized in Brazil

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The present study provides information about the bioaccessible fraction of aluminium (Al) in 16 samples of infant formulas using an optimized *in vitro* digestion method and inductively coupled plasma optical emission spectrometry (ICP OES). The bioaccessibility varied from 3.0% to 34% and the minimum and maximum values of Al in the bioaccessible fraction were 18.66–29.22 μg kg⁻¹, 36.60-71.48 μg kg⁻¹ and 19.60–160.2 μg kg⁻¹ for starters, follow up and specialized infant formula samples, respectively. The bioaccessibility varied between the analyzed infant formulas depending on sample composition, ingredients, age consumption indications, food matrix (dietary fat and fiber), food processing, co-ingested food and nutrient availability status.

**Keywords:** Infant Formula; Bioaccessibility; Aluminium; Food Analysis; in Vitro Digestion Method; Inorganic Contaminants.
INTRODUCTION

Human milk is the optimal source of nutrition for infants (Boquien, 2018; Picciano, 2017) and, in general, poor breastfeeding practices have been associated with higher risks of infectious disease and morbidity in developing and developed countries (Heymann, Raub, & Earle, 2013; Stuebe, 2009). In the last decades, infants have been offered infant formula from the first month due to its convenience, ready availability and due to medical conditions that prevent the mother from nursing (Nabulsi et al., 2014). Infant formulas are liquids or re-constituted powders that infants consume as replacements for, or supplementary to, breast milk. They are typically produced from animal or plant sources and are mostly dairy-based or soy-based food products (Bermejo et al., 2000). Infant formula is the major source of nutrients for many infants and a unique source of food during the first months of life (Bermejo et al., 2000; Rodríguez Rodríguez, Sanz Alaejos, & Díaz Romero, 2000).

However, the existence of pollutants and toxic metals, such as aluminium (Al), in infant formula may put children’s health at risk (Paiva et al., 2019). Human exposure to toxic metals, especially infants, has increased significantly due to urbanization, industrialization and greater anthropogenic emissions. The combination of infants’ lower body weight, immature kidneys and liver, decreased capacity of detoxification and vulnerability of the myelin central nervous system make infants particularly susceptible to toxic substances (Dhamo & Shabani, 2014; Landrigan et al. 2003; Hulin et al., 2014). Moreover, human exposure to Al is identified as a possible contributor to neurodegenerative / neurodevelopmental diseases, such as multiple sclerosis and Alzheimer’s disease (Ahmed, et al., 2016; Mold, 2018).

Aluminum is the third most abundant element in the earth’s crust (8%) and the first amongst the metals. Due to its elevated reactivity, it is found combined with oxygen to form its main ore, bauxite (Al₂O₃), as well as in the form of silicates, oxides and hydroxides and it is also found as a component naturally present in potable water and in additives composed of Al salts combined with other elements such as sodium and fluorine, and complexed with organic material (Hardisson & Gonzaléz, 2017; Cozzolino, 2005).

The European Food Safety Authority (EFSA) established a Tolerable Weekly Intake (TWI) for Al of 1 mg/kg body weight (bw) (EFSA, 2008), whilst in its 74th meeting, the Joint FAO/WHO Expert Committee on Food Additives (JECFA) confirmed the value of the PTWI (Provisional Tolerable Weekly Intake) for Al as being 2 mg/kg bw, which is applied to all the Al compounds in foods, including food additives (FAO/WHO, 2011; CAC, 2018). JECFA observed that the PTWI is likely to be exceeded in some population groups, particularly children, who regularly consume foods containing Al-based additives or ingredients. The Committee also inferred that exposure to this metal by infants fed infant formulae is high and recommended further investigations with these products. In a recent study, Paiva et al.
(2019) reported the total Al concentrations in infant formulas commercialized in Brazil, with important findings regarding Al exposure of newborns and infants.

Therefore, due to the relevant concern about Al toxicity, and considering the particular features of infants to Al exposure, better food control strategies are needed, especially those destined for children. Additionally, the information about inorganic constituents usually indicates the total concentrations to be ingested and not the amount that will be effectively absorbed by the body. This type of information could be provided by studies of bioaccessibility (the amount of the element that is released into the gastrointestinal tract from its matrix) and bioavailability (the fraction of the element which is absorbed from the gastrointestinal tract by the human organism, reaches the bloodstream and is then used in biological functions) (Minekus et al., 2014; Machado et al., 2017; Peixoto et al., 2016).

The interest in bioaccessibility of chemical elements has been growing in recent years, and many of them have been assessed in different food matrices, such as baby food (Do Nascimento da Silva et al., 2013; Do Nascimento da Silva et al., 2018), cereal products (Fu and Cui, 2013; Khouzam et al., 2011; Laparra et al., 2007; do Nascimento da Silva et al., 2013; Peixoto et al., 2016; Bhatia et al., 2013; Domínguez- González et al., 2010; Vitali et al., 2008; Yang et al., 2014), biscuit (Vitali et al., 2008), lettuce (Do Nascimento da Silva et al., 2015), beef (Menezes et al., 2018), coffee (Alongi et al., 2019), berries (Pereira et al., 2018) and cheese (Ayala-Bribiesca et al., 2017; Khouzam et al., 2011), using different experimental models of in vitro digestion.

Some important issues have been addressed in the literature such as the influence of food structures and the synergism or antagonism between food components, as well as the standardization of methods to evaluate the soluble fractions of a food during the gastrointestinal digestion. However, bioaccessibility studies of Al are still limited with regard to food for infants and children (Souza et al., 2019; Pereira et al., 2018; Melø et al., 2008; Khalifa & Ahmad, 2010) and no information was found in the literature concerning data on Al bioaccessibility in infant formulas. Therefore, the aim of the present work was to evaluate the bioaccessible fraction of Al in this type of product using an optimized in vitro digestion method followed by optical emission spectrometry with an inductively coupled plasma source (ICP OES).

**MATERIAL AND METHODS**

Material, reagents and equipment

All of the reagents used in the research were of or above analytical grade. Water (18.2 MΩ.cm) was purified with reverse osmosis (Gehaka, São Paulo, Brazil) while nitric acid (HNO₃) purification (Distillacid, Berghof, Eningen, Germany) was achieved with a sub-boiling
distiller. Hydrogen peroxide ($\text{H}_2\text{O}_2$) 30% (m/v) was provided by Merck (Darmstadt, Germany) in order to perform total Al mineralization. A certified 100 mg L$^{-1}$ standard solution (Specsol, Quimlab, Jacareí, Brazil) in a 0.5% HCl solution (v/v) (Merck, Darmstadt, Germany) was used to prepare the analytical curves. Two certified reference materials were employed to evaluate the method accuracy: egg powder (EGGS-1, National Research Council, Canada) and a diet (Typical Diet, NIST SRM 1548a).

The following reagents were used for the bioaccessibility assay: sodium hydrogen carbonate (NaHCO$_3$, >99.7 %), alpha-amylase (saliva solution) from Aspergillus oryzae (30 U mg$^{-1}$), lactase (85,300 USP), pepsin porcine gastric mucosa (>250 U mg$^{-1}$), bile from bovine and ovine (bile acid mixture) and pancreatin from porcine pancreas (8 x USP) (Sigma-Aldrich, Saint Louis USA). A dubnoff shaking water bath (NT 230, Nova Técnica, Piracicaba, Brazil) and a pHmeter (Starter 3100, Ohaus, Parsippany, EUA) were also used in the experiments.

**Samples**

A total of 16 samples of infant formulas was acquired in the city of Campinas, SP, Brazil from distinct batches and different brands (designated as A to D). The samples were stored in a dry place at room temperature (25 °C) and the main ingredients contained in the products are shown in Table 1. The digestion *in vitro* assay was performed in all referred samples, which were selected among the products considered in the present study to represent specific matrix composition for infant formulas. All measurements of the bioaccessible fraction of Al were performed in triplicate and the results were expressed as percentages.
Table 1. Description of common ingredients of infant formulas according to the consumption indication and composition.

<table>
<thead>
<tr>
<th>Sample composition</th>
<th>Ingredients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Starter formulas</strong></td>
<td>Lactose, Whey protein concentrate, Palm olein, Skimmed milk, Palm kernel oil, Canola oil, Corn oil, Calcium citrate, Potassium chloride, Potassium citrate, Magnesium chloride, Sodium citrate, Ferrous sulfate, Zinc sulfate, Copper sulfate, Potassium iodide, Manganese sulfate, Sodium selenite, Vitamin C, Vitamin E, Niacin, Calcium pantothenate, Vitamin A, Vitamin B6, Vitamin B2, Vitamin D, Vitamin B1, Folic acid, Vitamin K, Biotin, Fish oil, Soy lecithin, Arachidonic acid, L-arginine, L-carnitine, Nucleotides, Taurine, Choline bitartrate, Inositol.</td>
</tr>
<tr>
<td><strong>Follow up formulas</strong></td>
<td>Skim powdered milk, Corn syrup solids, Lactose, Palm oil, Coconut oil, Soybean oil, Sunflower oil, Mixture of arachidonic acid from M. alpina oil and Docosahexaenoic acid from C. cohnii oil, Calcium carbonate, Sodium citrate, L-Ascorbic Acid, Maldextrin, Choline chloride, Dibasic Magnesium Phosphate, Ferrous sulfate, Taurine, Potassium citrate, D-alpha-tocopheryl acetate, Cytidine 5-monophosphate, Zinc sulfate, Retinyl palmitate, L-Ascorbic Acid, Nicotinamide, Myo-inositol, Colecalciferol, Acid 5-monophosphate disodium salt, F美妙moniodine, Adenosine 5-monophosphate, Guanosine disodium 5-monophosphate, D-calciu...</td>
</tr>
<tr>
<td><strong>Specialized formulas</strong></td>
<td>Mal...</td>
</tr>
<tr>
<td><strong>Without lactose</strong></td>
<td>Skim powdered milk, Corn syrup solids, Lactose, Palm oil, Coconut oil, Soybean oil, Sunflower oil, M. alpina oil, Calcium carbonate, Sodium citrate, L-Ascorbic Acid, Maldextrin, Choline chloride, Dibasic Magnesium Phosphate, Ferrous sulfate, Taurine, Potassium citrate, D-alpha-tocopheryl acetate, Cytidine 5-monophosphate, Zinc sulfate, Retinyl palmitate, L-Ascorbic Acid, Nicotinamide, Myo-inositol, Colecalciferol, Acid 5-monophosphate disodium salt, F美妙moniodine, Adenosine 5-monophosphate, disodium salt of guanosine 5-monophosphate, Choline bitartrate, L-carnitine, Taurine, Potassium hydroxide.</td>
</tr>
<tr>
<td><strong>Iron fortified</strong></td>
<td>Mal...</td>
</tr>
<tr>
<td><strong>Soy-based</strong></td>
<td>Mal...</td>
</tr>
</tbody>
</table>

Determination of total Al

A sample of 1.0 g of reconstituted infant formula (3.0 g powder dissolved in 20 mL of water) was weighed into a digestion flask and 8 mL of purified HNO₃ plus 2 mL H₂O₂ were added and maintained in contact overnight according to the described method optimized by Paiva et al. (2019). The total Al concentration was determined in the reconstituted infant formula sample.
Determination of Al bioaccessibility

Dialysis method

The *in vitro* digestion model was performed according to Perales et al. (2006), considering the gastrointestinal system of the infant with some adaptations. The quantities and concentrations of the enzymes solution were optimized taking into account the gastrointestinal capacity of the infant. Approximately 10 mL of reconstituted infant formula with water were transferred to clean erlenmeyer flasks and mixed with water to a final volume of 20 mL. The pH of the samples was adjusted to 7.0 and 4 mL of saliva solution were added for salivary digestion. The mixture was incubated at 37 °C in a shaking water bath for 5 min. Thereafter, the samples were acidified to pH 2.0 with 6 mol L\(^{-1}\) hydrochloric acid (HCl) with addition of 0.3 mL of a porcine pepsin preparation (1.6 g of porcine pepsin in 10 mL 0.1 mol L\(^{-1}\) HCl). The mixture was incubated at 37 °C in a shaking water bath for 2 h. To stop the gastric digestion phase, the samples were maintained for 10 min in an ice bath. The gastric digest solution added by pancreatin-bile was titrated with 0.5 mol L\(^{-1}\) NaHCO\(_3\) solution to determine the volume of base needed to increase the pH to about 7.5. Dialysis bags (Sigma-Aldrich, Saint Louis, EUA, with cut-off from 12.000 to 16.000 Da and porosity of 25 Å), containing 20 mL of freshly prepared 0.5 mol L\(^{-1}\) NaHCO\(_3\) solution and water, were immersed in the pepsin digests and incubated in a shaking water bath at 37 °C. After 30 min, 0.75 mL of pancreatin-bile salt mixture (0.4 g porcine pancreatin and 2.52 mg bile bovine per 100 mL of 0.1 mol L\(^{-1}\) NaHCO\(_3\)) were added and incubated in a shaking water bath at 37 °C for more 2 h. The samples were maintained in the ice bath for 10 min to stop intestinal digestion. Dialysates were transferred for weight to graduate tubes and used to determine Al as previously described.

Determination of the optimum concentration of NaHCO\(_3\)

The optimum dialysis concentration of NaHCO\(_3\) was calculated using titratable acidity (Shiowatana et al., 2006). Titratable acidity was defined as the number of equivalents of NaOH required to titrate the amount of digest to a pH of 7.5. It was determined using standard 1 mol L\(^{-1}\) NaHCO\(_3\) as titrant. This concentration of NaHCO\(_3\) changed the pH of the dialysate to 5.0–6.0 after 30 min of dialysis and gradually increased the pH to 7.0–7.5 on the addition of pancreatin-bile extract.
Method validation for Al quantification in infant formula

Accuracy, repeatability, linearity, detection limit (LOD) and quantification limit (LOQ) were evaluated according to the National Institute of Metrology, Standardization and Industrial Quality (INMETRO, 2017) and reported by Paiva et al. (2019).

For the concentration range from 2 to 200 µg L⁻¹ of Al, a satisfactory correlation coefficient value was found (r²>0.999), showing the linearity of the analytical curve. The LOD and LOQ were determined using 10 replicates of an analytical blank, multiplied by the sample dilution factor (8.3 x). The values found for infant formulas were: LOD (3 s) = 16 µg kg⁻¹ and LOQ (5 s) = 30 µg kg⁻¹, with “s” being the standard deviation value of the 10 blank replicates.

In order to determine the repeatability of the method, the intra-day coefficients of variation (CV) were evaluated in different samples of infant formula (n=8). The mean value found was 8% satisfying the conditions recommended by the Official Methods of Analysis (AOAC, 2013) with a maximum CV of 25% for the range concentration. The accuracy of the method was evaluated in two certified reference materials (CRM): Typical Diet (SRM 1548a - Typical Diet) and Egg Powder (NRC EGGS - Egg Power) with results varying from 87% to 97%, in accordance with the AOAC (2013) guidelines, which establish a range from 75 to 120%, for the studied concentration.

RESULTS

The results obtained for Al bioaccessibility (%) in infant formula samples from different commercial brands are displayed in Table 2, which also presents the Al total content and the concentration in the dialyzed fraction. Total Al concentrations in infant formula samples were previously discussed by Paiva et al. (2019).

It was observed that the highest levels of Al in the bioaccessible fraction were present in specialized formula brand B iron fortified (160.2 µg kg⁻¹), followed by follow up brand B (95.96 µg kg⁻¹) and brand A (83.56 µg kg⁻¹), and soy-based brand A (55.49 µg kg⁻¹). The lowest observed value was present in starter infant formula brand C (18.66 µg kg⁻¹).

The findings show that the bioaccessibility for all analyzed samples varied from 3% to 34%, which may be related to the composition and characteristics of each sample. For starters formulas, the evaluated samples presented bioaccessibility ranging from 8.5% to 13%. For follow up samples, the range obtained varied from 4% to 20%, and among specialized infant formulas the found bioaccessibility values were 19% for the sample without lactose, 34% for the iron fortified, whilst for soy-based ones the observed range was between 3% and 11%.
Table 2. Total Al content, Al in the bioaccessible fraction and bioaccessibility (expressed as % of total concentration) in infant formulas.

<table>
<thead>
<tr>
<th>Consumption indication</th>
<th>Brand</th>
<th>Number of samples</th>
<th>Total Al (μg kg⁻¹)</th>
<th>Bioaccessibility</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Bioaccessible fraction (μg kg⁻¹)</td>
<td>%</td>
</tr>
<tr>
<td><strong>Starter</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>1</td>
<td>296 ± 0.4</td>
<td>29.22 ± 3.1</td>
<td>10</td>
</tr>
<tr>
<td>B</td>
<td>1</td>
<td>231 ± 25</td>
<td>25.02 ± 1.7</td>
<td>8.5</td>
</tr>
<tr>
<td>C</td>
<td>1</td>
<td>206 ± 3.4</td>
<td>18.66 ± 3.1</td>
<td>9.0</td>
</tr>
<tr>
<td>D</td>
<td>1</td>
<td>195 ± 4.7</td>
<td>24.97 ± 0.3</td>
<td>13</td>
</tr>
<tr>
<td><strong>Follow up</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>2</td>
<td>353 ± 3.2</td>
<td>27.63 ± 1.6</td>
<td>8.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>410 ± 4.1</td>
<td>83.56 ± 2.0</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td></td>
<td>337 ± 76</td>
<td>47.01 ± 3.9</td>
<td>14</td>
</tr>
<tr>
<td>B</td>
<td>2</td>
<td>492 ± 3.8</td>
<td>95.96 ± 1.2</td>
<td>20</td>
</tr>
<tr>
<td>C</td>
<td>1</td>
<td>179 ± 20</td>
<td>36.60 ± 2.8</td>
<td>20</td>
</tr>
<tr>
<td>D</td>
<td>2</td>
<td>975 ± 102</td>
<td>43.52 ± 0.4</td>
<td>4.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>919 ± 73</td>
<td>54.81 ± 1.8</td>
<td>6.0</td>
</tr>
<tr>
<td><strong>Specialized formulas</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iron fortified</td>
<td>B</td>
<td>1</td>
<td>468 ± 36</td>
<td>160.2 ± 9.4</td>
</tr>
<tr>
<td>Without lactose</td>
<td>C</td>
<td>1</td>
<td>253 ± 11</td>
<td>49.41 ± 8.8</td>
</tr>
<tr>
<td>Soy based</td>
<td>A</td>
<td>1</td>
<td>510 ± 28</td>
<td>55.49 ± 4.1</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>1</td>
<td>678 ± 155</td>
<td>19.60 ± 0.8</td>
</tr>
<tr>
<td></td>
<td>D</td>
<td>1</td>
<td>557 ± 21</td>
<td>41.27 ± 2.8</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Table 2 shows the different samples analyzed, mean Al concentration in the bioaccessible fraction, standard deviations, and bioaccessible percentage obtained for Al in standard infant formulae (cow milk-based), specialized and soy-based considering the indications for consumption.

The obtained mean values of Al in the bioaccessible fraction for starter, follow-up and specialized formulas were 24.46 μg kg⁻¹, 53.38 μg kg⁻¹ and 65.19 μg kg⁻¹ respectively. Higher values were found for follow up and specialized formula compared to starter ones and this may be due to the greater variety of composition and additional ingredients. The higher mean contents found in some specialized formulae suggest that the need to greatly modify the raw material with aggressive treatments (such as protein hydrolysis) can result in a greater exposure of the product to a larger amount of Al during manufacture due to the...
addition of chemicals and contact with machines and powder particles (Navarro-Blasco & Álvarez-Galindo, 2003).

In the current literature, few studies are related to the bioaccessibility of contaminants, especially Al in infant foods. In a recent study conducted by Souza et al. (2019), the Al bioaccessible fraction of corn flour, rice and oat, and rice cereals was determined. Only a multigrain cereal sample presented Al concentration of 1.04 mg kg\(^{-1}\) in the dialysable fraction, which corresponds to 6% of bioaccessibility and is similar to the obtained value for brand D follow up formula (6%) in the present study. \(^{a}\)Paiva et al. (2020) also determined the Al bioaccessible fraction in infant cereals and found low values for multicereals varying from 2.2% to 5%. Those values are comparable with the current percentages obtained for soy-based brand C (3%) and follow up brand D (4%) infant formulas.

Pereira et al. (2018) evaluated the bioaccessible fraction of some minerals including Al present in some berries produced in São Paulo state, Brazil such as blackberry, raspberry, blueberry and strawberry, obtaining Al fractions in percentage of 3%, 2.4%, 33% and 4%, respectively (expressed as % of total concentration). \(^{b}\)Paiva et al. (2020) found the bioaccessible fraction in infant foods varying from 0.5% to 48% according to the sample composition (salty purees, fruit purees, infant drinks and petit suisse).

Studies on the digestibility and absorption of phytonutrients such as vitamins, carotenoids, polyphenols, curcuminoids, polyunsaturated fatty acids, proteins, peptides, dietary fibers, oligosaccharides and minerals have shown, according to Thakur et al. (2020), that phytonutrient bioaccessibility has been further enhanced by the addition of oil, fat and certain enzymes. Moreover, the group states that the bioaccessibility depends on food matrix (dietary fat and fiber), food processing, co-ingested food and nutrients status. Therefore, the distinct composition and required ingredients of infant formulas may explain the difference in Al bioaccessibility observed between the samples.

Theoretical calculations were used in a study by Do Nascimento da Silva et al. (2015) to determine the hydration energies of the polyphenols and the binding energies of the cellulose monomer and polyphenols to the metals in order to better understand the effects of certain matrix components on the bioaccessibility of chemical components. The obtained results were also consistent with the concept of hard and soft acids and bases (HSAB), which indicates that Al\(^{3+}\) and Fe\(^{3+}\) are hard acids. Therefore, Al\(^{3+}\) and Fe\(^{3+}\) are less polarizable compared to other metals, and polyphenols and cellulose contain OH\(^{-}\) and RCOO\(^{-}\) groups, which are hard bases. Thus, the interactions of fiber sources (cellulose) and polyphenols with Fe\(^{3+}\) and Al\(^{3+}\) tend to be more stable than the interactions of these compounds with Zn\(^{2+}\) and Cd\(^{2+}\), for example (Shriver, 1999). The strongest interaction of Al with cellulose may explain the fact that in spite of high total Al content, previously determined by \(^{b}\)Paiva et al.
the samples presented low bioaccessibility, especially those containing soy, such as brand C (3.0%) and brand D (7.0%).

In addition to their binding energies, Do Nascimento da Silva et al. (2013) also calculated the hydration energies of the polyphenols to evaluate the solubility of these compounds. Thus, the correlation between the amount of polyphenols and the Al bioaccessibility from different baby foods could be determined. It was observed that lower polyphenol content means a greater interaction between the elements and less soluble structures, such as proteins, fibres and phytates, which leads to smaller bioaccessible fractions. The low bioaccessible fraction observed in Table 2 for starters infant formulas may be strongly related to the large amount of proteins. In this regard, it is interesting to note that, in general, starter infant formulas present lower bioaccessible fraction compared to the follow up ones due to the larger amount of proteins, once that the label declares the presence of whey protein concentrate in their composition. Nevertheless, the high bioaccessibility showed by iron fortified (specialized formula, 34%) might be explained due to presence of skimmed milk instead of whole milk or protein concentrate. Although the theoretical results show that the interaction between Al and polyphenols is the strongest, which would lead to greater bioaccessibility for this element, its interaction with cellulose is also the strongest. The interaction with cellulose may be the most important factor governing the bioaccessibility of elements in foods that contain larger amounts of cellulose than polyphenols. In addition, the cellulose structures are less soluble, which will more strongly affect the bioaccessibility of Al.

Further, some studies have associated low mineral absorption with the presence of antinutritional factors, such as phytates, which are present in plant seeds, grains and, at high amounts, in wheat bran, acting as the main stored form of phosphate in plant seeds (Paiva et al., 2019; Do Nascimento et al., 2015). Regarding total Al content and its bioaccessible fraction, some parameters must be taken into account, such as the element forms (different chemical compounds), the behavior of organometallic species and complexes in the gastrointestinal tract, and the interactions with the food matrix (Khouzam, Pohl, & Lobinski, 2011).

CONCLUSIONS

In the present study, it was possible to determine the Al bioaccessible fraction of infant formulas through an adapted in vitro approach considering the gastrointestinal system of children. The highest Al bioaccessible fraction content was observed in specialized infant formulas followed by follow up samples, with mean bioaccessibility values varying from 3% to 34% depending on the sample ingredients and composition. The findings highlight the importance of assessing Al exposure given that the inclusion of other foods in the diet can increase its overall intake, which may represent a health concern, especially for frequent
users. The data obtained in this study will contribute to the global assessment of potential health risks associated with Al exposure, suggesting the need to identify ways of monitoring the quality of ingredients used in infant food production and to establish research to explain the mechanism of toxicity associated with Al.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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REFERÊNCIAS


18. Fu, J. & Cui, Y. (2013). In vitro digestion/Caco-2 cell model to estimate cadmium and lead bioaccessibility/bioavailability in two vegetables: the influence of cooking and additives. Food and Chemical Toxicology, 59, 215–221. https://doi.org/10.1016/j.fct.2013.06.014


