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Occurrence and determination of inorganic contaminants in baby food and infant formula

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Inorganic contaminants, including those commonly known as 'heavy metals' (cadmium, arsenic, lead and mercury) and others like aluminum, copper, zinc, and nickel, may be present in baby foods such as infant formulas, cereals, snacks, prepared meals, and jarred fruits and vegetables. Children, babies and toddlers are more vulnerable to these toxic elements due to their immature development and high 'food intake/body weight' ratio. The most important adverse effects of inorganic contaminants for infants include: anemia, nephrotoxicity, developmental, and reproductive toxicity, lower intelligence quotient (IQ), and neurotoxic effects. As this topic represents a relevant food safety issue, this article aims to review recent data about the occurrence of inorganic contaminants in baby foods, regulatory aspects, exposure assessment, as well as analytical methods for their determination. The available information reinforces the importance of standardizing routine quality control and reducing inorganic contaminants levels in infant formula and baby foods.

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Introduction

According to the World Health Organization, adequate nutrition during infancy and early childhood is essential to ensure the growth, health, and development of children to their full potential [1]. Global recommendations for optimal infant feeding include exclusive breastfeeding for six months and nutritionally adequate and safe complementary feeding starting from the age of six months with continued breastfeeding up to two years of age or beyond [2]. Milk formulas are usually recommended as human milk substitutes when breastfeeding problems occur [3••].

It is well known that raw materials used to prepare foods intended for infants and young children, such as milk, vegetables, fruits, and cereals, may contain a number of chemical elements with toxic properties [4•]. Moreover, inorganic contaminants may also arise from further processing of these materials, which may compromise the safety of baby foods [5]. These include elements commonly known as 'heavy metals' (cadmium, arsenic, lead, and mercury) and others like aluminum, copper, zinc and nickel [6].

The potential toxic effects of these elements in infants and young children are well documented in the literature and include decrease of intelligence quotient IQ and deficiencies in the development of nervous, reproductive, digestive, respiratory, and immune systems. Moreover, children are more susceptible to the exposure to contaminants than adults due to their high intestinal absorption capability and low effective excretion [3••,7]. Consequently, this topic is of significant interest to the public health and should be carefully addressed. Therefore, the aim of this study is to review recent data about the occurrence of inorganic contaminants in baby foods, regulatory aspects, exposure assessment as well as analytical methods for their determination.

Toxicity of inorganic contaminants

The toxicity of metals can be discussed in terms of chronic or acute effects. Most metals have a high affinity with the sulfhydryl group of proteins and can inhibit more than two hundred enzymes in the biological system [4•]. Long-term exposure to toxic metals induces adverse effects in many organs of the human body, such as hepatonephrotoxicity and neurotoxicity [6].

Chemically, metals in their ionic form can be very reactive and interact with biological systems in a wide variety of ways, considering that a cell has numerous ligands for binding to chemical elements. Metals can show more specific forms of interactions through mimicry, for example. By acting as essential metal mimics, they attach to physiological sites that are normally reserved for an essential element. Another important chemical reaction in the toxicology of metals is the oxidative damage mediated by these elements. Many metals may act directly as catalytic centers for oxidoreductive reactions with molecular oxygen or other endogenous oxidants, producing oxidative modifications of biomolecules such as proteins and DNA. This may be the major stage in the carcinogenicity process of certain metals. In addition to oxygen-based radicals, carbon and sulfur radicals can occur [8]. The toxicity mechanism in children depends on the exposure frequency to a specific metal. However, toxic effects such as pediatric pneumonia, neurological disorders, and altered neuro-behavioral development are the most reported in literature [9•].

According to the Joint FAO/WHO Expert Committee on Food Additives (JECFA), there is no safe exposure level to lead [10]. However, although the removal of this element from house paint and gasoline has reduced the occurrence of lead in the environment, contamination remains [11,12]. Lead is a classical chronic or cumulative poison that can result in a wide range of adverse effects in humans depending upon the level and duration of exposure [13••]. Health effects are generally not observed after a single exposure. Lead has been shown to be associated with impaired neurobehavioral functioning in children [13••]. Inorganic lead compounds are classified by the International Agency for Research on Cancer (IARC) as probably carcinogenic to humans [13••].

Cadmium is classified as a carcinogenic metal and its presence in the environment is mostly considered as a by-product. Cadmium is not found as a pure metal in nature and high concentrations have been observed in association with lead and zinc ores [14,15]. In 2010, JECFA replaced the Provisional Tolerable Weekly Intake (PTWI) of 7 $\mu g\,kg^{-1}$ body weight (bw) and recommended a Provisional Tolerable Monthly Intake (PTMI) of 25 $\mu g\,kg^{-1}$ bw [10]. IARC classified cadmium and cadmium compounds in group 1 (carcinogenic to humans) [13••].

Arsenic is ranked by the Agency for Toxic Substances and Disease Registry (ATSDR) as number one on the Priority List of Hazardous Substances, and it is classified by IARC as a human carcinogen (group 1) [16]. For the general population, drinking water is the major source of exposure to arsenic followed by fish consumption, in which high levels occur as non-toxic arsenobetaine, as well as cereals, in which arsenic occurs as toxic inorganic forms [10]. In 2010, JECFA withdrew the PTWI of 15 $\mu g\,kg^{-1}$ bw of inorganic arsenic recommended in 1988 once it was no longer appropriate [10,17].

Mercury is a severe environmental problem with adverse effects on living organisms and ultimately on human beings [18]. The organic fraction, represented mainly as methylmercury (MeHg), is a potent neurotoxin which has shown x of effects on fetal growth and neurocognitive development in early childhood [19,18]. In 2010, JECFA establish the PTWI of 4 $\mu g\,kg^{-}$ bw for inorganic mercury, and in 2006 confirmed the PTWI value of 1.6 $\mu g\,kg^{-1}$ for methylmercury [13••].

Exposure to aluminum has been associated with anemia, impairment of bone formation and neurotoxic effects such as Alzheimer's disease. Recent studies have also shown that human exposure to aluminum is identified as a possible contributor to multiple sclerosis. Individuals with relapsing remitting multiple sclerosis (RRMS) and secondary progressive multiple sclerosis (SPMS) were shown to excrete large amounts of aluminum in their urine, an observation recently built upon and confirmed in individuals with SPMS [20].

Small quantities of copper and zinc are essential for hematopoiesis and other physiologic processes; however, large amounts of copper intake causes hepatic necrosis and sometimes death [21]. Nickel has been detected in water, air, soil, and dust; however, through inhalation, an iota of ingestion becomes inevitable in total daily exposure. Associations between nickel and lung cancer constitute the main cause of concern [22].

Occurrence of inorganic contaminants in infant foods, regulatory aspects and health risks

Natural phenomena, such as volcanism, and anthropogenic activities play an important role in transporting and spreading chemical elements in the environment, which results in their accumulation in the food chain [23]. Metals are not subjected to the biodegradation process and, once released into the environment; they are adsorbed by sediments and biomagnified in the food chain [24].

In general, the main sources of inorganic contaminants in infant food are related to water and soil contamination, ingredients, and addition of inorganic salts during processing [25]. The concentration of metals in natural waters varies significantly depending on numerous physico-chemical, mineralogical, and geochemical factors [5].

Table 1 shows the concentrations of some inorganic contaminants in baby foods recently reported in literature. Data were available in several countries, such as France [26], Tanzania [27•], United States [28,29], Switzerland [30], Brazil [4•], and Australia [31]. Levels of arsenic varied from 0.014 to 0.228 $mg\,kg^{-1}$ and were higher in products containing rice (rice grains, rice cereals, rice crackers/biscuits). Concentrations of cadmium were in the range 0.002–0.022 $mg\,kg^{-}$ with the highest levels also observed in rice. The lowest levels of lead were found in baby foods from the United States

Table 1

Occurrence levels of inorganic contaminants in baby foods (mg kg^{-1}).

Food	As	Cd	Pb	Al	Cu	Hg	MeHg	Zn	Ni	Country/ Reference
Milk-based beverage	-	-	-	-	-	0.00050	-	-	-	France [26][a]
Cereals-based food	-	-	-	-	-	0.00058	-	-	-	
Milk-based dessert	-	-	-	-	-	0.00058	-	-	-	
Fruit juice	-	-	-	-	-	0.00050	-	-	-	
Growth milk	-	-	-	-	-	0.00050	-	-	-	
Soup puree	-	-	-	-	-	0.00050	-	-	-	
Fruit puree	-	-	-	-	-	0.00050	-	-	-	
Vegetable-based ready-to-eat meal	-	-	-	-	-	0.00050	-	-	-	
Meat/fish-based ready-to-eat meal	-	-	-	-	-	0.00080	-	-	-	
Infant formula	-	-	-	-	-	0.00050	-	-	-	
Follow-on formula	-	-	-	-	-	0.00052	-	-	-	
Skimmed milk powder	-	0.003	0.020	2.2	0.439	-	-	45.7	0.080	Tanzania [27•][b]
Full cream milk	-	0.002	<0.010	1.85	0.054	-	-	28.0	0.030	
Infant formula	-	0.002	<0.010	1.0	0.410	-	-	39.6	0.050	
Dry baby milk	-	-	0.0255-0.0744	-	0.9-6.5	-	-	-	0.0326-0.0814	Turkey [38][c]
Infant food	-	-	0.0482	-	1.0-4.9	-	-	-	0.0711-0.1151	
Infant biscuit	-	-	0.0155-0.0644	-	0.8-5.8	-	-	-	0.0501	
Various (organic)	-	0.0056	0.0097	-	-	-	-	-	-	USA [28][d]
Various (non-organic)	-	0.0056	0.0093	-	-	-	-	-	-	
Rice grains (brown)	0.205	-	-	-	-	-	-	-	-	Switzerland [30][e]
Rice grains (white)	0.143	-	-	-	-	-	-	-	-	
Baby food dry form	0.083	-	-	-	-	-	-	-	-	
Baby food ready-to-eat	0.014	-	-	-	-	-	-	-	-	
Milk rice	0.015	-	-	-	-	-	-	-	-	
Rice cereals	0.228	-	-	-	-	-	-	-	-	
Rice crackers	0.169	-	-	-	-	-	-	-	-	
Rice drinks	0.019	-	-	-	-	-	-	-	-	
Baby biscuit	-	-	-	1.2	-	-	-	-	-	Turkey [39][e]
Baby fruit puree	-	-	-	1.3	-	-	-	-	-	
Rice	-	-	0.56-0.97	1.9-13.8	1.81-2.7	-	-	13.2-17.0	-	Brazil [4•][c]
Rice and oat	-	-	0.49-0.74	7.13-16.0	1.88-3.83	-	-	14.4-83.0	-	
Multicereals	-	-	0.95-0.99	2.77-17.1	1.48-2.48	-	-	64.2-141.0	-	
Corn flour	-	-	1.06-2.63	1.3-5.75	0.59-1.46	-	-	89.0-107.0	-	
Breakfast cereal	-	<0.01	<0.01-0.03	-	-	-	-	-	-	Australia [31][b,c]
Rice	-	<0.01-0.022	<0.01-0.014	-	-	-	-	-	-	
Rice baby cereal	0.190	-	-	-	-	0.002	0.00062	-	-	USA [29][e]
Rice teething biscuit	0.097	-	-	-	-	0.007	0.00094	-	-	
Oat or wheat baby cereal	0.021	-	-	-	-	0.00023	0.00001	-	-	
Pre-cooked milled baby-food rice and rice cakes	-	-	-	-	-	0.00185	0.00171	-	-	United Kingdom [19][e]

N, number of samples; ND, Not detected.

[a] Upper bound average values.

[b] Median values.

[c] Range for individual samples (minimum–maximum).

[d] Infant formula, cereals, kids' meals, toddler formula, juices/drinks, jars/first meals, pouches, snacks, and electrolyte solutions. Concentrations refer to 75th percentile.

[e] Mean values.

Table 2

Maximum limits for inorganic contaminants (mg kg^{-1}).

Contaminant	Food	Brazil [32]	China [33]	Codex Alimentarius [13••]	European Union [34,35]	USA [36]	New Zealand [37]
Inorganic As	Cereal-based baby food	0.15	0.2	-	-	0.1	
	Infant formulas and follow on-formulas	0.02	-	-	-	-	-
	Other foods specially formulated for infants and young children	0.02	-	-	-	0.01	-
Lead	Cereal-based baby food	0.05	0.2	-	0.05	-	-
	Infant formulas and follow on-formulas	0.01	0.15	0.01	0.01 – 0.05[a]	-	0.02
	Other foods specially formulated for infants and young children	0.01	-	-	-	0.005	-
Cadmium	Cereal-based baby food	0.05	-	-	0.04	-	-
	Infant formulas and follow on-formulas	0.01	–	-	0.005 – 0.02[b]	-	-
	Other foods specially formulated for infants and young children	0.01		-	-	-	-

[a] Infant formulas and follow on-formulas considering the liquid (0.01 mg kg^{-1}) and powder (0.05 mg kg^{-1}) forms.
[b] Infant formulas and follow on-formulas considering the liquid formulae manufactured from cows' milk proteins or protein hydrolysates (0.005 mg kg^{-1}) and powdered formulae manufactured from soya protein isolates, alone or in a mixture with cows' milk proteins (0.02 mg kg^{-1}).

(0.0093–0.0097 mg kg^{-1}), while the highest amounts were reported in Brazil (0.49–2.63 mg kg^{-1}). Concentrations of aluminum varied from 1.0 to 17.1 mg kg^{-1} and the highest levels were also observed in Brazil (rice and oat, multi-cereals). Copper and nickel were found in the ranges 0.05–6.5 mg kg^{-1} and 0.03–0.115 mg kg^{-1}, respectively, while zinc showed higher amounts (13.2–141.0 mg kg^{-1}). Very low levels of mercury and methylmercury were reported (0.01–7 μg kg^{-1}).

Table 2 presents maximum limits for contaminants such as arsenic, lead, and cadmium in baby foods, infant formulas and other products, according to regulatory agencies from Brazil (ANVISA) [32], China [33], Codex Alimentarius [13••] European Commission [34,35], USA [36], and New Zealand [37]. In a study developed with Brazilian infant cereals [4•], a range of 0.95–0.99 mg kg^{-1} of lead was obtained, which is higher than the maximum limit of 0.05 mg kg^{-1} established by the Brazilian, Chinese, and European Commission regulatory agencies. Samples of rice baby cereal [29], rice grains (brown), rice cereal and rice crackers [30] presented mean arsenic levels of 0.19 mg kg^{-1}, 0.205 mg kg^{-1}, 0.228 mg kg^{-1}, and 0.169 mg kg^{-1}, respectively, which is above the maximum limit of 0.15 mg kg^{-1} allowed in Brazil and 0.1 mg kg^{-1} in USA. Regarding other foods specially formulated for infants and young children, one sample of infant food [38] showed lead concentration of 0.0482 mg kg^{-1} that surpasses the maximum limit of 0.01 mg kg^{-1} according to ANVISA [32], but is acceptable for USA maximum limit of 0.005 mg kg^{-1}. No sample of infant formula among those presented in Table 1 showed levels above the maximum limits for lead, arsenic, and cadmium [39,31].

Exposure assessment to inorganic As for toddlers (1–3 years) was reported considering the 95th percentile of food consumption [30]. The highest intake (0.118 μg kg^{-1} bw day^{-1}) was estimated to be via rice grains consumption, when maximum concentration and exposure via drinking water are taken into account. The estimated dietary intake of methylmercury was performed in the United States considering four age groups – four, six, nine, and twelve months [29]. In the referred study food matrix such as rice baby cereals, rice-containing teething biscuits, and wheat/oat cereals were analyzed, for which the average exposures (μg kg^{-1} day^{-1}) were 0.0011, 0.00082, and 0.000019, respectively. All values fell below the reference dose of 0.1 μg kg^{-1} day^{-1}. A further American study regarding the contamination of infant formula with lead and cadmium demonstrated that none analyzed sample would exceed the Food and Drug Administration (FDA) provisional limit of 6 μg day^{-1} for lead while 22% would exceed the daily intake limit set by California's Proposition 65 (0.5 μg day^{-1}). For cadmium, 14% of formulas would exceed the limit of 5.3 μg day^{-1} (WHO tolerable daily limit for a 6.4 kg baby), while 23% would exceed the Proposition 65 daily limit of 4.1 μg day^{-1} [28].

Analytical methods for determination of total level of inorganic contaminants

The monitoring of inorganic contaminants at trace levels for food, biological and environmental purposes are extremely desirable and essential. Various analytical techniques are used and these methods can be classified as spectrometric, chromatographic and electrochemical methods. An overview of the main analytical methods used in recent studies for the determination of inorganic contaminants in baby foods is shown in Table 3.

The evaluation of the elemental composition of organic or inorganic matrices requires sample preparation approaches that include partial or total dissolution of the sample before instrumental analysis. These involve digestion of the matrix, extraction, and preparation of the analytes. Sample digestion methods such as dry or wet decomposition in open or closed systems, using thermal,

Table 3

Analytical methods for the determination of inorganic contaminants in baby foods.

Matrix	Method	Contaminant	Reference
Composite food samples	Microwave digestion and inductively-coupled plasma-mass spectrometry (ICP-MS)	Aluminium (Al), antimony (Sb), arsenic (As), barium (Ba), cobalt (Co), chromium (Cr), gallium (Ga), germanium (Ge), lead (Pb), mercury (Hg), nickel (Ni), silver (Ag), strontium (Sr), tellurium (Te), tin (Sn), vanadium (V).	[3••,45]
Baby foods, prepared with meat, fish, vegetables, cereals, legumes, and fruits	Hydride-generation atomic-fluorescence spectrometry	Antimony (Sb), arsenic (As), bismuth (Bi), and tellurium (Te)	[16]
Dry baby milk, dry baby milk with fruit, infant food with fruit and infant biscuit	Inductively coupled plasma optical emission spectrometry (ICP OES)	Cu(II), Ni(II) and Pb(II)	[40]
Infant formulas, follow-on formulas and baby porridges	Atomic absorption spectrometry (AAS) equipped with a graphite furnace (GF) for electrothermal atomization	Arsenic (As), lead (Pb), cupper (Cu), and tin (Sn)	[42,43,44]
Baby biscuit, baby food and baby fruit puree	Fluorimetry	Aluminium (Al)	[20]
Water and juice	UV–Visible spectrophotometry	Inorganic arsenic (As)	[46]

ultrasonic, or radiant (infrared, ultraviolet, and microwaves) energy tools are essential for the digestion of inorganic substances, before their analysis [40,41].

In general, the most applied analytical techniques for inorganic contaminants are conventional spectrometric methods namely flame atomic absorption spectroscopy (FAAS) [42–44], inductively coupled plasma optical emission spectrometry (ICP OES) [38], inductively coupled plasma mass spectrometry (ICP-MS) [3••,28,30,45], and atomic fluorescence spectroscopy [16]. Fluorimetry and UV–vis spectrophotometry were also reported in literature for Al and As quantification in baby biscuits, fruit purees, water, and juice [39,46].

The use of tandem MS with the ICP technique not only provides a decrease in solvent volumes, higher throughput, and improved resolution, but also allows speciation methods for inorganic contaminants; however, the main disadvantage related to this technique is the high cost [47]. Flame atomic absorption spectroscopy, fluorimetry, and UV–vis spectrophotometry are more affordable price techniques; however, they present low analytical sensitivity when compared to mentioned techniques, such as ICP OES and ICP-MS [48].

Nanotechnology and functional materials with submicron size and distinct physiochemical characteristics have recently opened up new horizons for food safety inspection and generated a large number of methods of detection with improved analytical performance and further, may contribute with better performance for the analysis of the complex sample matrices [49,50].

Conclusions

Occurrence of inorganic contaminants in foods intended for infants and young children, as reported in several recent studies, indicates a health concern and the need to establish or strength management measures to reduce this contamination. A greater data collection, the monitoring of water quality, soil, raw materials and final products, and exposure assessments conducted around the world could provide information to support risk management strategies. Advances in analytical methods were noted, but mostly validated procedures were only available for the determination of total levels of these elements. In this sense, future challenges may include contaminants speciation and their possible interactions with other compounds in the matrix, which could directly affect the bioavailability. Improved communication among stakeholders is a key need and consumer demands for a safer product can provide food manufacturers with the oft-requisite economic incentive necessary to take steps toward reductions of inorganic contaminants content in baby foods and infant formulas.

Conflict of interest statement

Nothing declared.

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