International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

A Review on the Toxicological Elements of Commercial Pediatric Food and its Long-Term Bodily Effects

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DOI: https://doi.org/10.55248/gengpi.2022.3.5.23

Abstract

Commercial food has been an essential part of any pediatric individual's diet since the minerals and vitamins help sustain their dietary requirements and is given as early as being a newborn. However, it also contains toxicological elements which are associated with long-term bodily effects. These elements can be essential and non-essential. Essential elements found in pediatric food given as early as infancy play a part in the development of pediatric individuals. On the other hand, non-essential elements which include the heavy metals and other toxins may have long-term effects with their brain development. Pediatric individuals, but most especially newborns, infants, and young children are the most vulnerable to these contaminants since their brain and organ systems are yet undeveloped. This article aims to identify the long-term bodily effects and the risk factors of toxicological elements found in commercial pediatric food, which will either hinder or suppress the proper growth of these individuals.

Keywords: Toxicological, Commercial Pediatric Food, Long-term Effects

Introduction

Throughout infancy and early childhood, it is critical to provide adequate nutrition to ensure a child's full growth, health and development, through the breast milk of their mother [1]. However, corresponding to the growing gap in the nutrients from breast milk and the increasing nutritional requirements of a growing child, complementary feeding is introduced. The World Health Organization (WHO) supports this further [2], wherein they have provided that an infant requires to have enough stamina and nourishment to be that cannot be provided by breast milk as they grow further, thereby requiring complementary foods for their growth's sustenance. In connection to this, by the moment infants become fit enough for complementary feeding, commercial pediatric food is thereby introduced.

As children grow older, pediatric foods that are commonly available commercially have become an important part of children's diet because of the ingredients that help in fulfilling their dietary requirements. Although made for young individuals, the intake of such actually comes with a risk especially that raw materials that contain toxicological elements may perhaps be utilized in the preparation of these products [3]. Accordingly, these toxic elements may also be attributed to product contamination during its production, as well as its packaging. Due to the physiological characteristics of children, especially those that have not reached adolescence yet, these products make them highly vulnerable to the possible toxicological elements of these foods. Specifically, infants and young children have a higher sensitivity to toxins because their metabolic rates are higher during these ages [4].

Consequently, commercial pediatric food, especially those that are formulated for the first 2 months and 12 years of life, should be a source of nutrition and free from toxic substances. These products should be a supplement to their growth and development, not hinder it. Therefore, the goal of this paper is to be able to assess literature on various toxicological elements found in commercial infant and baby food and their long-term bodily effects on infants and young children.

Methodology

Recent studies, peer-reviewed articles, and journals from ResearchGate, Science Direct, Google Scholar, CrossRef, PubMed, Sage Journals, and other databases were used for this review article. The articles reviewed and synthesized focus on the toxicological elements of various commercial infant and baby food and their long-term bodily effects. These gathered pieces of evidence that are systematically organized and evaluated, will be helpful in filling the gaps in the research. A repeated review is done in the manuscript for suitable changes prior to finally approaching any journal database.

1. Essential Elements found in Commercial Infant and Baby Food

Both essential macro and microelements are important in pediatric development. In infants and toddlers, when important biochemical processes are being formed, hindering development may have long-term effects on their bodies. Due to this, the ample amount of essential elements should be provided to help ensure the development and prevent unforeseen deficiencies [5].

Essential macro-elements, as provided, include Ca, Na, P, K, Cl, Mg, and S. Two of these essential elements, including calcium and phosphorus, are important in pediatric growth as they both have a role in skeleton development as well as bone mineralization. Apart from both, magnesium is also involved in bone development, along with other different bodily processes such as pathway signaling, energy storage and transfer, glucose and lipid metabolism, functioning of the neurological and muscular systems [5].

Essential trace elements, on the other hand, involve Fe, Cu, Zn, Se, I, Cr, Co, and Mo. Beginning with iron, this element serves a role in oxygen transport and energy metabolism [6]. One of the most notable manifestations of deficiency of iron is anemia, which is known to have negative effects on energy. Iodine is another essential trace element, known to have an importance in the thyroid hormone attributed to its ability to bind with receptors helpful in the regulation of various important processes in the body including metabolism, growth and neurologic functions [7]. Another important trace element is selenium, commonly found in its selenoprotein form which helps in immunity improvement and resistance to oxidative stress [8].

2. Non-Essential Elements found in Commercial Infant and Baby Food

Non-essential elements such as lead, cadmium, and other toxins are contaminants found in baby food which may affect their brain development. Baby foods bought by the consumers from the market contain a concentration of toxic elements such as antimony (Sb), arsenic (As), and bismuth (Bi)[9]. Heavy metal contamination inclusive of are harmful in any amount, despite its diminutiveness in these formulations.

Infants and young children are those that are especially vulnerable to these contaminants attributed to the fact that their brains and organ systems are not yet fully developed during these ages. Consumer reports have stated that an exposure even in small quantities of these toxicants at young age has the possibility of having various health problems involving lower intellect and complications regarding the behavior, with associations to autism and attention deficit disorder. These may also cause other long-term effects and are irreversible due to its linkage with the bladder, cognitive and reproductive problems, among other conditions known and unknown [10].

3. Toxicological Elements of Various Commercial Infant and Baby Food

3.1 Heavy Metals

Commercially-recognized pediatric foods, including formulas, snacks, fruits, and vegetables made suitable for children in young ages may contain heavy metals [11], having any unknown purpose or nutritional value for the human body, as stated by Bradl et al. Generally, humans regardless of their ages, may it be known or unknown to them, can be exposed to these substances through the ground water, volcanic ash, erosion, forest fire, emissions in a factory, and uncontrolled pollution [12]. These heavy metals can induce adverse effects such as anemia, nephrotoxicity, neurotoxicity, lack of development of the nervous system, reproductive system, gastrointestinal system, respiratory system, immune system and as well as reduced intelligence quotient [11].

3.1.1 Arsenic (As)

Naujokas et al. provides in Tyler et al. [13] that arsenic is a naturally-derived metalloid, a toxin, and a known agent that aggravates the carcinogenic effects of other substances, and induces cognitive dysfunction even in small amounts. It exhibits several mode of action that impart toxicity including effects on epigenetic profiles by depleting methyl groups, oxidative phosphorylation uncoupling and reactive oxygen species escalation, inhibiting enzymes that contain thiol and proteins, glutathione depletion, cell proliferation and alteration of signal transduction, and genotoxicity by reducing repair of DNA, as reported by Hughes et al. Inorganic arsenic (iAs) targets the liver through induction of metalloids of numerous mechanisms of liver damage like inflammation, oxidative stress, and activation of cell death [14]. In addition, it changes memory and learning and influences neurogenesis and cholinergic neurobiological processes, glutamatergic, and monoaminergic system pathways [13].

Epidemiology studies support that higher risk of diabetes development can be experienced due to iAs-toxicity exposure. However, its mechanism of action in diabetes pathogenesis is still being assessed. Arsenic dysfunctions β-cells by direct cell damage and functional deregulation. Furthermore, it targets the hematologic system by hemolytic and apoptotic effects. It also affects the innate and adaptive immune responses through deregulation of immune regulators, immune cells apoptosis, damaging macrophages, and activating lymphocytes, as described by the research of Dangleben et al. [14]

A research from Australia also revealed that greater than 53% of one baby rice-based products surpassed the intended 0.1 mg kg^{-1} maximum level of As according to the European Union and Islam et al. Zhao et al. claim that this is due to the high level of As absorption or high-affinity arsenic uptake system of rice. Moreover, Signes-Pastor, Carey, & Meharg explained in their study that baby foods made from rice are regularly used by young children because of its mild taste, fortification, and not likely to cause allergic reactions. Hence, children are more vulnerable to excessive concentrations of As. For instance, studies in various countries reported that exposure of children to arsenic is high due to baby rice products, according to Llorente-Mirandes et al. However, As guidelines for this susceptible group only arose in 2016 by the European Union [15].

3.1.2 Lead (Pb)

This is known for its neurotoxic effects that cause lower IQ, learning problems, permanent effects on nervous system development. It is the second most toxic metal next to Arsenic and its half-life is greater in children. A study by Jannat et al. have shown that its concentration in baby foods are lower than standard regulatory levels but its presence continues to be a concern, as stated by Oskarsson et al., because babies are more susceptive to toxicants' effects due to their underdeveloped organs that increase chemical gastrointestinal absorption [16]. The increased use of lead in industrialization and in products for agriculture, oil, paint, and mining are the cause of it contaminating the environment; hence, entering the food chain. Its toxicity can be exhibited by several mechanisms such as enzyme inhibition, damaging the antioxidant cell defense system, affecting the Mg, Ca, and Zn homeostasis, elevate levels of blood enzyme, mineralization of teeth and bones [17], DNA transcription interference [18], and protein synthesis reduction [17]. It damages the activity of polymorphonuclear leukocytes cells that lowers immune response, hinders the enzymes that aid in the vitamin D synthesis, and the enzymes that support cell membrane integrity. It also affects the biosynthesis of heme by damaging the enzyme activity of delta-aminolevulinic acid dehydratase, claimed by Patrick et al. [18].

As mentioned by Fang et al., it is transported to the hepatic system, which produces oxidative imbalance, ER stress from impairment of the proteins [18], and chronic toxicity effects and to the kidneys where it will damage its structure and change the excretory function, according to Yuan et al. [17]. In addition, Casarett et al. specified that lead can induce toxic effects in infants' brain through obstructing the formation of the synapse in their cerebral cortex, affecting neurochemical growth, and damaging neuron myelin sheaths, which is also stated by the authors Pearson and Schonfeld. Kosnett also added that the abnormal behavior symptoms of lead poisoning may vary from person to person [18]. The maximum tolerated dose of lead for infants and toddlers is 0.5 µg/day and its interim admissible intake for a week is 25 µg/kg/bw, in conjunction with the suggestion of WHO et al. [19]

3.1.3 Mercury (Hg)

According to Lavoie et al., this non-essential element is toxic even in low concentrations and is a known carcinogen and for its bioaccumulative characteristic [20]. It can be found at around 0.5 parts per million in the earth's crust, which outgasses from rock and volcanic activity; thus, leading to exposure to humans. Species convert atmospheric elemental mercury in water into organic mercury that can be ingested by fishes [21]. Humans can primarily be exposed to it through food ingestion, as claimed by Bose-O'Reilly et al. However, according to Choi et al., too much consumption can lead to disruption of nervous, cardiovascular, renal, and reproductive systems. WHO announces that the interim admissible weekly intake of inorganic mercury and organic mercury are 4.0 μg/kg and 1.6 μg/kg b.w., respectively, as suggested by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) [20]. Moreover, the EFSA or the European Food Safety Authority approved a bearable intake for a week of methylmercury at 1.3 μg/kg b.w. [22]. The NHANES or the National Health and Nutrition Examination Survey announced that children in the United States under the age of 10 consume approximately 0.33 μg of Hg/kg b.w. per day, higher than the consumption of adults which is 0.05 μg/kg bw/day [20].

Several studies have claimed that too much exposure to mercury causes alterations in the CNS, which results in irritability, lethargy, changes in the behavior, convulsions, headaches, loss of hearing and cognition, speech defects, incoordination, hallucinations, and death. It also induces hypertension and changes in endothelial function. Mercury toxicity can vary in condition with the structure, amount, and exposure rate. Methylmercury is mainly the cause of neurological changes in both humans and animals due to the elevated reactive oxygen species (ROS) and increased attraction for tubulin sulfhydryl groups which impede the microtubule arrangement essential in central nervous system development, according to Sager et al. On the other hand, Mottet et al. book revealed that inorganic mercury causes neuronal hyperpolarization by enhancing the chloride channels permeability of dorsal root ganglion gamma-aminobutyric acid A receptors. According to Hulthe & Fagerberg, mercury also inactivates an enzyme called paraoxonase, which is essential in antiatherosclerotic activity and reduces the oxidation process of LDL, as claimed by Halbach in an article. In addition, it enhances free radical development and reduces antioxidant enzyme activities of glutathione peroxidase [23].

3.1.4 Cadmium

This carcinogenic substance, as categorized by the International Agency for Research on Cancer (IARC), is present in the environment due to various human activities including fossil fuels, combustion of metal ore, and burning of wastes. It may be absorbed by plants and transferred in the food chain through leakage of sewage sludge to the soil [24]. A study in Poland by Kot, Zareba, & Wyszogrodzka-Koma claimed that potatoes, grains, cereals, and other plants have the highest concentration of Cd. Upon ingestion, its deposition is mainly in the liver and kidneys. However, it remains a significant hazard to infants because of their nervous system underdevelopment, its effects on the processes of bone-formation, and its known carcinogenic effects. Hence, evidence on the positive connection of Cd and autism are laid out, according to the IARC & Silbergeld [25]. Infants can be exposed to Cd through convenient foods, powdered formula, and cereal-based food, according to the EFSA. Hence, the organization suggested that the tolerable weekly intake (TWI) for cadmium is 2.5 μg/kg b.w., according to an EFSA journal. However, in 2010, the JECFA recommended a PTMI of 25 μg/kg b.w. due to its long half-life and daily effects upon exposure. 12 month old babies in Poland have been consuming more Cd than the TWI value settled by EFSA [22].

According to Rani et al., proliferation, differentiation and programmed cell death can be affected by cadmium [24]. It attaches to the mitochondria, which disrupts cell respiration as well as oxidative phosphorylation, and causes mutations. Moreover, its toxicity can be exhibited by depleting reduced glutathione, binding if SH groups with protein, and enhancement of ROS production leading to oxidative stress. It also hinders the antioxidant activities of catalase, manganese-superoxide dismutase, and copper/zinc-dismutase enzymes, as stated in the article of Filipic. Specifically, Cd affects the skeletal system through affecting calcium metabolism and Vitamin D3 and causes skeletal demineralization, which impedes the production of collagen and procollagen C-proteinase. Cd can induce renal cardiovascular system damage. Intoxication would result in endothelial dysfunction, thrombogenic events, cytokine production, hypertension, and lipid peroxidation in the brain [24].

3.1.5 Aluminum

The eating behavior of infants reached a turning point with the rising and development of complementary food. It is quite popular with the public that some infant foods contain potentially toxic elements and some do not. One example is aluminum which is commonly found in water, minerals and soils. There are numerous studies or evidences wherein infants and fetuses are more sensitive to pollutants such as Aluminum. The metabolic pathway of children is immature and especially the first months after birth and was also hinted that their metabolism and detoxification are not the same with the adults in terms of efficiency. Multiple diseases are linked with the exposure of humans to Al which are considered a possible contributor, not only does it contribute to neurodevelopmental/neurodegenerative diseases but also Alzheimer's disease and multiple sclerosis (MS). Studies show that an individual with relapsing remitting multiple sclerosis (RRMS) and secondary progressive multiple sclerosis (SPMS) were identified to discharge huge amounts of aluminum in their urine and human subjection to Al was also linked with the disability of anemia and bone function [11,26].

Infant drinks with soya and chocolate composition have been found to exhibit highest Al levels as 23 countries were chosen in Central and South America, East and West Africa and Asia where it was found that in the 61 samples of chocolates and cocoa beans, the concentration yield differentiated from 10.6 mg kg^{-1} in Central America and 21.5 mg kg^{-1} in South America whereas the difference between Central America and East Africa were 41 mg kg^{-1} and 275 mg kg^{-1} respectively

[27]. In terms of Al contamination, adding cocoa powder to newborn products should be avoided as the values stated above shows that cocoa products possibly contribute to Al contamination in foods.

3.1.6. Nickel

In pre-made infant foods, nickel is generally present and a short-term nickel intake can cause allergic reactions in individuals that are sensitive towards nickel either through direct contact or through dietary intake. Nickel in food is commonly caused by its accumulation in the sediments along areas wherein it relocates to the crops like nuts, pules, oilseeds, vegetables and cereal-based products. Although nickel is mainly found in the soil. To add, processing and preservation is another source of contact as some companies use steel products that contain nickel in processing food. Although nickel intake is dangerous, an evaluation of the available sources of data can give way to a detailed and in-depth understanding of the situation and a risk assessment protocol and preparation can be made [28].

A study investigated the average Lower Bound and Upper Bound chronic exposure to nickel across the different dietary surveys and age classes. Grain-based products, which are commonly found in baby food, were the most necessary cause to the mean LB chronic dietary exposure to nickel. The average of LB and UB chronic dietary exposure of tolerable daily intake (TDI) in toddlers was around 12.5/14.6 μg/kg bw per day which is at the level of the TDI, indicating a health problem. The 95th percentile LB exposure surpassed the TDI in 10 out of 14 dietary surveys in toddlers, as well as in 11 out of 19 surveys in other children. Moreover, an excess TDI was observed in some surveys of infants. In adolescents and in all adult age groups, the 95th percentile LB chronic dietary exposure was lesser than the TDI. Therefore, the 95th percentile chronic exposure to nickel can be a health concern for infants, toddlers and other children [29].

3.1.7 Copper

Small quantities of copper are essential in hematopoiesis or the formation of blood cellular components and other physiologic processes. Little is known about the bioavailability of copper as it is recently added to many infant formulas and copper deficiency has not been observed in preterm and term infants fed with human milk [11,30]. This element, when consumed above the recommended amount can prove to be detrimental to the cell and its components. Abnormal amounts of copper can cause DNA damage, oxidative stress and decreased cell growth [31]. Reactive oxygen species and the build-up of ionic copper forms that bombard the capacity of protein binding are among the causative factors for the element's toxicity [32].

3.1.8 Zinc

Zinc is essential for human body well-functioning, a cofactor, and a mineral important so that the body can produce enzymes. Exposure and toxicity with zinc are common since its sources are abundant in the environment. It can become toxic if greater concentrations are introduced to the human body [33]. This element is commonly added in baby foods. A study revealed that the concentration of zinc in infant food was increased than the formulas for infants [16].

Acute toxic effects of zinc compounds when ingested will mainly include gastrointestinal symptoms and hematemesis because of their direct caustic toxicities. Moreover, reported incidence of renal damage such as hematuria, interstitial nephritis, or acute tubular necrosis have been noted. Accordingly, the pathophysiological process of zinc toxicity is not completely known, but some authors believed that cellular damage from the nanoparticles of zinc triggers an immune inflammatory response, which results in flu-like manifestations and local damage of tissue. In addition, the chronic toxicity affects the bone marrow and causes polyneuropathy because of accompanying copper insufficiency [34]. The Recommended Dietary Allowance (RDA) of zinc for infants is 2 to 3 mg, while children aged 1 to 3 years old is 3 mg [35].

3.2 Acrylamide

This inorganic compound is created when low moisture foods are made ready at greater than 120 ºC, particularly with asparagine and reducing sugars (e.g glucose and fructose) in foods [36] or starchy cuisines like potato and grains, as stated by Dybing et al. [36]. It is toxic to the reproductive system and a known substance that exhibits carcinogenic, genotoxic, neurotoxic, hepatotoxic, and immunotoxic effects [37]. In addition, its neurotoxic effects can be manifested by peripheral and central neuropathy, drowsiness, or cerebellar ataxia due to neurotransmission direct inhibition, changes in the cells, key enzyme inhibition, and kinesin-based fast axonal transport bonding [38].

3.3 Bisphenol A

Bisphenol A (BPA) is usually used as a plasticizer, as well as a monomer in the polycarbonate synthesis. It is also used to form linings in most canned food and drinks which include containers for liquid infant formula, among others. It is a chemical that disrupts endocrine and is almost commonly found daily. A study by Cok et al. [39] has found out that among different communities, the presence of BPA in children is higher than that of young and full grown adults.

BPA is also said to be associated with estrogen receptors (ER) by functioning as an agonist or antagonist through ER dependent signaling pathways because of its phenolic structure as provided by Konieczna et al. [40]. Attributed to this are findings that support BPA being able to have a part in the pathogenesis of some disorders regarding the endocrine.

3.4 Dioxins

Dioxins are considered an environmental pollutant. They belong to a group of persistent organic pollutants (POPs). They last for a long period of time inside the body since they can be absorbed by the fat tissue, where they stay and get stored [41]. High levels of dioxin are found in the environment, especially in soils and food involving milk, meat, and fish. On the other hand, they are less likely to be found in plants, water, and air. Half-lives of dioxins range from 7 to 11 years; environmental dioxins in the food chain are agglomerated where the levels determine the concentration of dioxin (higher position means higher exposure, vice versa).

Dioxins are a concern to the health of the society due to its high toxicity. The most sensitive to dioxin exposure are the developing fetus. There are 419 types of dioxins identified, with 30 of which are considered to have susceptibilities for toxicity as stated by the World Health Organization [41].

3.5 Furan

In a natural occurring substances found in food such as vitamins (e.g., ascorbic acid), macronutrients (e.g., carbohydrates, amino acids, unsaturated fatty acids), and carotenoids. Furans and their related compounds (2- and 3- methyl furans) involves a high risk to infants which are said to be the most exposed group, through the consumption of commercial foods as stated by the European Food and Safety Authority (EFSA).

In the liver, Furan is metabolized to form cis-2-butene-1,4-dial by the enzyme cytochrome P450. This active metabolite has potential acute toxicity to liver cells. Furan rings will undergo cleavage through oxidation and form very reactive radical cations of furan or epoxides, which would then interact with the nucleophiles of the cell. The metabolites will damage DNA or cellular proteins that produce disarrangement of functions of the cell, as well as cell death. Long-term cell death and regeneration due to exposure of chronic furan can be a serious factor of the chemical's carcinogenicity [42,43].

3.6 Mycotoxins

Mycotoxins are made by a variety of molds including genera *Aspergillus, Fusarium, and Penicillium* that can grow on food in specific conditions and as well as have ill effects on people especially to children which are more susceptible to its toxic effects since they have lower body mass, a higher metabolic rate and children does not yet possess mature detoxification system. Routes of exposure to mycotoxins include ingestion, contact, and inhalation. Some mycotoxins cross the placenta and are found in the fetus at birth, others are eliminated through the milk [44].

Results and Discussion

1. Long-Term Bodily Effects of Toxic Heavy Metals

Dosing, as well as the route where the exposure was perceived, along with the exposure's duration, either acute or persistent, are the basis of heavy metal toxicity that results in numerous disorders and enormous damage because of free radical formation induced oxidative stress. The normal functions of the brain, lungs, renal, liver, composition of the blood, and other organs will be damaged. Moreover, long term effects are cancer and slow physical, muscular, and neurological progression of degenerative processes, which can emulate other diseases [45].

Mahurpawar [43] provided a tabulation (figure 1 and 2) containing clinical aspects of these toxicities that are manifested when heavy metals are depicted in food that are being taken by humans, especially infants and babies.

Metal	Target Organs	Primary Sources	Clinical effects
Arsenic	Pulmonary Nervous System, Skin	Industrial Dusts, Medicinal Uses Of Polluted Water	Perforation of Nasal Septum, Respiratory Cancer, Peripheral Neuropathy: Dermatomes, Skin, Cancer
Cadmium	Renal, Skeletal Pulmonary	Industrial Dust And Fumes And Polluted Water And Food	Proteinuria, Glucosuria, Osteomalacia, Aminoaciduria, Emphysemia
Chromium	Pulmonary	Industrial Dust And Fumes And Polluted Food	Ulcer, Perforation of Nasal Septum, Respiratory Cancer
Manganese	Nervous System	Industrial Dust And Fumes	Central And Peripheral Neuropathies

Figure 1. Clinical Effects of Heavy Metal (As, Cd, Cr, Mn) Toxicities and its Primary Sources, as provided by Mahurpawar et al. [46]

Lead	Nervous System, Hematopoietic System, Renal	Industrial Dust And Fumes And Polluted Food	Encephalopathy, Peripheral Neuropathy, Central Nervous Disorders, Anemia.
Nickel	Pulmonary, Skin	Industrial Dust, Aerosols	Cancer, Dramatis
Tin	Nervous , Pulmonary System	Medicinal Uses, Industrial Dusts	Central Nervous System Disorders, Visual Defects And EEG Changes, Pneumoconiosis.
Mercury	Nervous System, Renal	Industrial Dust And Fumes And Polluted Water And Food	Proteinuria

Figure 2. Other Clinical Effects of Heavy Metal (Pb, Ni, Sn, Hg) Toxicities and its Primary Sources, as provided by Mahurpawar et al. [46]

Another study by Parker et al. [47] has provided a table on the oral toxicity criteria upon heavy metal ingestion through baby food, due to its possible cancer and non-cancer risks. Figure 3 and 4 provide data on its traits according to the criteria of EPA, IRIS, and OSF, wherein results have shown in the cancer aspect that the inorganic arsenic is able to cause a tumor type called splenic sarcoma, alongside lead being able to cause kidney tumors. Accordingly, in the non-cancer occurrences of diseases, organs are compromised as provided—inorganic arsenic targeting cardiovascular and dermal organs, cadmium for urinary organs, inorganic mercury for kidneys, and lead for reproductive organs [47].

Heavy Metal	Cancer				
	Criterion	Value	Unit	Tumor Type	Reference
As, inorganic	EPA IRIS OSF	1.50E+00	$(mg/kg/day)^{-1}$	Splenic sarcoma	[38]
Cd	NA	NA	NA	NA	NA
Hg, inorganic	NA	NA	NA	NA	NA
Pb	Cal/ OEHHA OSF	8.50E-03	$(mg/kg/day)^{-1}$	Kidney tumors	[46]

Figure 3. The Cancer Criteria for Oral Toxicity by Heavy Metals by Parker et al. [47]

Non-Cancer				
Criterion	Value	Unit	Most Sensitive Target Organ/ System	Reference
EPA IRIS RfD	3.00E-04	mg/kg/day	Cardiovascular[a], Dermal[b]	[38]
EPA IRIS RfD	1.00E-03	mg/kg/day	Urinary[c]	[44]
EFSA TDI	5.70E-04	mg/kg/day	Kidney[d]	[45]
Cal/OEHHA MADL	5.00E-04	mg/day	Reproductive	[47]

Figure 4. The Non-Cancer Criteria for Oral Toxicity by Heavy Metals by Parker et al. [47]

Given that these metals are not only found in the table's provided sources, this has posed long-term bodily effects on the development of infants and babies, as these are also found in the food they take, which will be elaborated in the latter part of this paper.

1.1 Arsenic

In an 2021 article by Kuzemchak [10], they have provided results on the Clean Label Project's food study in 2017, wherein results have shown that among 500 commercial infant and baby products, about 65 percent comprises arsenic; those that are labeled to be organic food have been found to have higher detectable levels of arsenic than those of conventional products.

Moreover, a 2021 report [48] has supplied findings on As content in commercial infant and baby food, being present in products by the following companies:

- Nurture (HappyBABY)

This particular company has delivered into the market various baby foods, however, tests have shown that their products have held about 180 parts per billion (ppb) inAs, refractory from the U.S. FDA being only 100 ppb, as stated by Matei [49].

- Hain (Earth's Best Organic)

The company's products are said to hold about 129 ppb inAs, also noncompliant to the U.S. FDA Standards. However, this company only assessed the ingredients it utilized rather than its marketed products—from this, it was discovered that Hain had used ingredients that had 309 ppb, at most.

- Beech-Nut

The institution has made use of ingredients in baby food with elevated levels of arsenic, as high as 913.4 ppb, which they defended to be used in addressing product characteristics (at an average of 300 ppb), specifically, the claimed softness of its crumbs.

- Gerber

Finally, another company that has arsenic-containing products involved Gerber, wherein sixty-seven (67) assemblages of rice flour had 90 ppb inAs, only ten (10) ppb less than the U.S. FDA Standard.

1.2 Lead

Chronic exposure to lead, another toxic element, would lead to mental retardation, pervasive developmental disorder (autism), hypersensitivity, learning disorders, emaciation, agitation, immobility, as well as damage in the brain and kidney. An article by Loria [50] has provided that the FDA did not specify lead content requirements for baby foods, therefore, its susceptibility to being used at high levels by various manufacturers. Lead is also deemed toxic to the brains of children, and no amount has been determined to be safe [10]. However, Loria [50] has emphasized that only five (5) ppb is acceptable in bottled water.

The 2021 report [45] has also specified products that contained significant lead levels, as provided herewith:

- Nurture (HappyBABY)

Apart from containing arsenic, this company also has significant levels of lead in their products to as high as 641 ppb. Regrettably, about 20% of its products have shown levels of lead not lower than ten (10) ppb.

- Beech-Nut

Products by this company have been observed to contain an average of about 887 ppb of lead—483 of which have shown levels exceeding five (5) ppb, 89 products being noted with more than fifteen (15) ppb lead, and 57 have shown lead levels higher than 20 ppb.

- Hain (Earth's Best Organic)

Hain's products have also shown unexpectedly elevated levels of lead, garnering to about 352 ppb wherein 88 of its products had an average of over 20 ppb, with six (6) having levels up to 200 ppb and higher.

- Gerber

This renowned company has also shown lead content in its products, as high as 48 ppb and as low as 20 ppb.

1.3 Mercury

On the other hand, the Environmental Protection Agency (EPA) [51] provided that high carcinogenic effects are described in mercuric chloride and methyl mercury toxicity. Moreover, all types of mercury affects the nervous system that will lead to alterations of brain functions, tremors, irritability, and vision or hearing problems.

Reports from the U.S. House of Representatives [48] have provided companies utilizing lead, wherein among four companies–Nurture (HappyBABY), Beech-Nut, Hain, and Gerber–only Nurture had been accredited to about 10 ppb Hg levels. Both Beech-nut and Hain (Earth's Best Organic) only had acceptable Hg levels; Gerber rarely had Hg in its products as well.

1.4 Cadmium and Aluminum

Cadmium, a highly nephrotoxic substance, causes hypercalciuria, kidney stones, bone mineralization, calcium metabolism interference, and lung damage. Accordingly, cadmium ingestion has been associated with various disorders such as renal failure, diabetes, cancer and neurological disorders [52]. The figure below provides the mechanisms of cadmium toxicity, as provided by Jaishankar et al. [45].

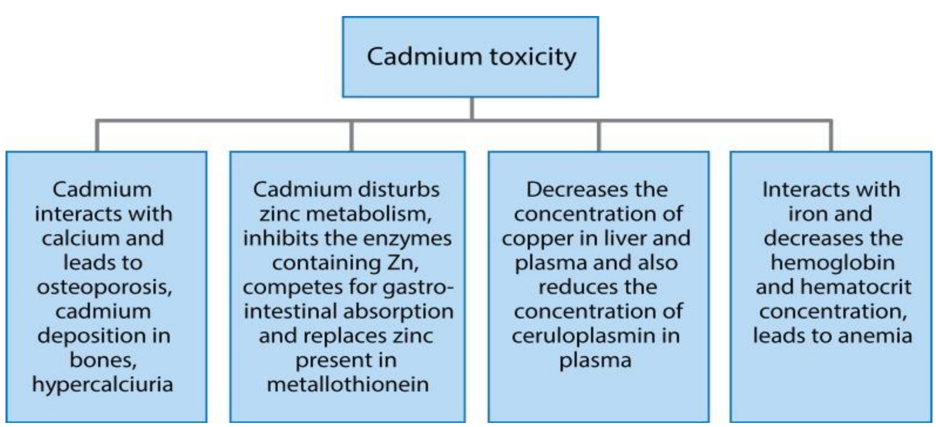

Figure 5. Cadmium Toxicity Mechanisms by Jaishankar et al. [45]

Cadmium has accordingly been depicted in various baby foods, as elaborated [48] herewith:

- Beech-Nut

  105 of its ingredients have been depicted to have over 20 ppb Cd, to as much as 344 ppb Cd.
- Hain (Earth's Best Organic)

  Ingredients amounting to 102 have had records of it containing Cd varying between 20-260 ppb.
- Nurture (HappyBABY)

  Sixty-five percent of this specific company's baby food products have been found to contain about 5 ppb.
- Gerber

  About seventy-five percent of Gerber's carrots contain more than 5 ppb cadmium, others containing up to 87 ppb.

On the other hand, aluminum exposure at high levels have been known to have induced various diseases, involving ulcers, and bone diseases (i.e. arthritis, adynamic bone disease and osteomalacia) [45]. With that being said, a study has shown that infant milk has been contaminated with aluminum [53] in ranges between 100-430 μg/L (wherein soya-based milk products had an average intake of 700 μg aluminum/day and non-soya-based formula had a range of 100-300 μg aluminum intake/day), much higher than the recommended by FDA only being 5 μg/kg/day for patients weighing over 50 kg [54].

1.5 Other Heavy Metals (Nickel, Copper, and Zinc)

Kuznetsova et al. [55] provided a tabulation on the copper, zinc, and lead content of various brands—Malyatko Premium 2, Bellakt 2, Nutricia's Malyuk Istrynsky 2 and Milupa 2, Nestle's NAN Optipro 2 and Nestogen 2, as well as Hipp Organic 2, as provided in the figure below:

Table 1 – The content of microelements in the baby milk *Malyatko Premium 2*

Chemical element	MAC, mg/kg	The content of the microelement, mg/kg	Excess of the microelement content, mg /kg
Copper (Cu)	0.5	0.57	0.07
Zinc (Zn)	5	5.45	0.45
Lead (Pb)	0.05	0.13	0.08

Table 2 – The content of microelements in the baby milk *Bellakt 2*

Chemical element	MAC, mg/kg	The content of the microelement in the baby food, mg/kg	Excess of the microelement content, mg /kg
Copper (Cu)	0.5	0.55	0.05
Zinc (Zn)	5	5.20	0.20
Lead (Pb)	0.05	0.1	0.05

Table 3 – The content of microelements in the baby milk *Nutricia Malyuk Istrynsky 2*

Chemical element	MAC, mg/kg	The content of the microelement in the baby food, mg/kg	Excess of the microelement content, mg /kg
Copper (Cu)	0.5	0.5	0.0
Zinc (Zn)	5	5.1	0.1
Lead (Pb)	0.05	0.05	0.00

Table 4 – The content of microelements in the baby milk *Nutricia Milupa 2*

Chemical element	MAC, mg/kg	The content of the microelement in the baby food, mg/kg	Excess of the microelement content, mg /kg
Copper (Cu)	0.5	0.49	- 0.01
Zinc (Zn)	5	4.9	- 0.1
Lead (Pb)	0.05	0.05	0.00

Table 5 – The content of microelements in the baby milk *Nestle NAN Optipro 2*

Chemical element	MAC, mg/kg	The content of the microelement in the baby food, mg/kg	Excess of the microelement content, mg /kg
Copper (Cu)	0.5	0.5	0.0
Zinc (Zn)	5	5	0.0
Lead (Pb)	0.05	0.05	0.00

Table 6 – The content of microelements in the baby milk *Nestle Nestogen 2*

Chemical element	MAC, mg/kg	The content of the microelement in the baby food, mg/kg	Excess of the microelement content, mg /kg
Copper (Cu)	0.5	0.5	0.0
Zinc (Zn)	5	4.95	- 0.05
Lead (Pb)	0.05	0.049	- 0.001

Table 7 – The content of microelements in the baby milk *Hipp organic 2*

Chemical element	MAC, mg/kg	The content of the microelement in the baby food, mg/kg	Excess of the microelement content, mg /kg
Copper (Cu)	0.5	0.5	0.0
Zinc (Zn)	5	5	0.0
Lead (Pb)	0.05	0.05	0.00

Figure 6. Microelement Content in Infant Formula as provided by Kutsenova et al. [55]

This figure shows that infant milk may contain lead, copper, and zinc as the major contaminants of such but of different concentrations depending on the raw materials utilized during manufacturing and its environmental situations. As this contamination is attributed from the presence of objects in the biosphere (plant and animal raw materials, metal salts), it is claimed important in this study to developing a quality and distribution monitoring system for such production to be able to provide people safe food, especially those in their crucial growth stage, like infants [53].

Supportively, a 2020 provides an evaluation on the risk of nickel presence in premade baby foods, including 26 ready-to-eat foods, 31 fruits, 8 desert varieties, and 20 paps, that 91.8% of these samples have contained nickel of about 225.7 μg kg−1—upon which belongs 50.1 fruit content and 40.2 ready-to-eat food content [56]. Based on the mean of these results, the tolerable daily intake (TDI) of copper as provided by EFSA being 2.8μg kg−1 b.w. was exceeded by children ages 2 years old, highlighting significant risk on children consuming ready-to-eat baby food.

On the other hand, Cu exposure in an extended timeframe may cause kidney and liver disruption, while nickel exposure can lead to cancers, heart disorders, and allergic reactions [46]. Finally, another writeup by Miles [57] provides that the excessive amount of zinc in the diet of the infant or a baby, most likely acquired from their vitamin supplements, have been shown to have adverse effects, involving loose bowel movement, nausea and vomiting, abdominal cramps, headaches, among others.

2. Other Harmful Toxicological Elements of Commercial Infant and Baby Food (Acrylamide, Bisphenol A [BPA], Dioxins, Furan, and Mycotoxins)

2.1 Acrylamide

High levels of acrylamide were found in infant foods, specifically non-cereals that are produced from veggies, surpassing suggested safe acrylamide values along with cereals [36]. In another study, snack food products for infants have higher concentration of acrylamide than jarred baby foods. A heightened level is discovered in potato chips as well as crackers and breakfast cereals for babies.

Chronic effects of acrylamide were due to oxidative stress that initiates apoptosis, elevated ROs production, and GSH oxidation. Inhibition of neuroblastoma and glioblastoma cell differentiation because of the said agent disrupts the nervous system [58].

Finally, in this figure, Mielech et al. provides data on the acrylamide levels on infants and toddlers, wherein in all countries specified, there were excess intake and/or exposure on children through their food, as well as a higher exposure of acrylamide in children as compared to adults [4].

Type of Contamination	Number of Samples	Type of Food Sample	Results	Country [Reference]
		CONTAMINANT CONTENT		
	141	[a] Infant food, [c] commercial food	7% exceeded the RfD	France [26]
Acrylamide	141	[a] Infant food, [b] commercial food for toddlers	Detected in 80% of samples, exceeded the RfD	France [27]
	70	[a] Infant food, [c] commercial food	Exceedance of RfD in baby food	Estonia [28]
		ESTIMATION OF INTAKE		
Acrylamide	2517	[a] Infant food and [c] commercial food	Exposure of children twice as high as that of adults	USA [25]
	111	[a] Infant food	Average intake by infants and children exceeded RfD	Poland [29]

Figure 7. Acrylamide Contaminant Manifestations in Infants and Toddlers through Food Intake, as provided by Mielech et al. [4]

2.2 Bisphenol A (BPA)

The possible health effects of BPA in infants and babies are connected to changes in their developing nervous system, including thyroid function, as well as the growth of the brain; behavioral development changes, involving hyperactivity are also observed [37,52].

Another study by Ellahi and Rashid [60] also provides data on how BPA affects children's health, wherein depressive, anxious, and hyperactive behaviors were also exhibited upon elevated exposure to such a substance; however, there is more prominence in girls than in boys. In contrast, depressed and hostile behaviors were shown in girls when exposed in BPA, with boys having sensitivity and violent tendencies in ages 3-5 due to prenatal exposure, as provided by Pereira et al. in the same study.

Moreover, one of its variants called the noncoplanar PCB has been found out to affect dopamine, serotonin, and acetylcholine; coplanar PCB has shown effects on thyroid hormones and glucocorticoids, with severe reverberations in people of younger ages including fetuses, infants, and children [58].

Ultimately, BPA is also unsurprisingly detected in various food [4], including infant formula, commercial children food, and food in jars for babies, with no excess in its contamination; only China did not show any level of BPA contaminant in infant formula, as provided in the following figure:

Type of Contamination	Number of Samples	Type of Food Sample	Results	Country [Reference]
		CONTAMINANT CONTENT		
Bisphenol A	154	[b] Commercial food for toddlers, [d] commercial food	Detected in 36% of infant food samples, no TDI exceeded	China [33]
	122	[a] Jarred infant food	Detected in 81% of samples, no MDL exceeded	Canada [30]
	103	Human milk and [c] infant formula	Detected in 38% of infant food samples, no RfD exceeded	Spain [31]
	76	[c] Infant formula	None detected	China [35]
	68	[c] Infant formula	No bisphenol exceedances, no RfD exceeded	India [34]
	50	[c] Infant formula	Detected in 60% of infant formula samples	Italy [32]

Figure 8. BPA Contaminants in Food for Children, as provided by Mielech et al. [4]

2.3 Dioxins

Brief elevated dioxin exposure is found attributed to lesions on the skin, with symptoms being attributed to chloracne and darkening of the skin in a patchy manner; it also is attributed to the altered liver function of persons. With regards to its prolonged exposure, it contributes to damage of the immune, nervous, endocrine, and reproductive systems [41].

Apart from that, Mielech et al. [4] provides that hypotonia, neurodevelopmental and behavioral disorders, a lower IQ, deafening, dermatological problems, thyroid hormone abnormalities, have been exhibited by dioxins. In figure 9, tolerable daily intake or TDi of babies are provided, wherein results show that dioxin exposure in babies through infant food and commercial food for children are noticeably elevated in France.

Type of Contamination	Number of Samples	Type of Food Sample	Results	Country [Reference]
		CONTAMINANT CONTENT		
Dioxins	163	Commercial food, human milk, infant formula	No exceedance of the upper limit of the standard	Greece [40]
		ESTIMATION OF INTAKE		
Dioxins	180	[a] Infant food, [b] commercial food for toddlers	TDI exceeded in children of 7–12 months by 4.5%, in 13–36-month- olds by 5.1–7.4%	France [41]
	63	[a] Infant food, [b] commercial food for toddlers	Consumption is below the TWI	Italy [42]
	60	[a] Infant food, [c] infant formula	No exceedance of the TDI in baby food	Germany [39]
	16	[a] Infant food	No exceedance of the TDI in baby food	Spain [37]

Figure 9. TDI of Dioxins in Infants and Toddlers, as provided by Mielech et al. [4]

2.4 Furan

Furans, with its routes of exposure being oral, transdermal, and inhalation, is said to cause pulmonary edema and bronchiolar necrosis. When absorbed within the body, it also has the possibility to cause central nervous system depression which could lead to narcosis and tonic seizures [42,43].

As seen in figure 10, this contaminant is said to have contaminated various children's food, with countries Poland and China having a higher exposure among infants than in adults, due to its availability in infant food and commercial food for children [4].

Type of Contamination	Number of Samples	Type of Food Sample	Results	Country [Reference]
		CONTAMINANT CONTENT		
Furan	134	[a] Infant food, [b] commercial food for toddlers	Furan found in 84% of samples	France [43]
	101	[b] Commercial food for toddlers	Contamination of 12% of samples	Taiwan [48]
		ESTIMATION OF INTAKE		
Furan	301	[a] Infant food	EDI exceeded reference dose	Poland [47]
	191	[b] Commercial food for toddlers, [c] commercial food	EDI about 3 times higher among infants than adults	China [45]
	78	[a] Infant food, [b] commercial food for toddlers	EDI 3.8 times higher among infants than adults	Belgium [46]
		EXPOSURE		
	230	[a] Infant food, [b] commercial food for toddlers	Medium exposure is not a health risk	Germany [49]
Furan	76	[a] Infant food, [b] commercial food for toddlers	Meat- and fish-based products potential risk for children	Spain [44]

Figure 10. Furan Contaminant in Children's Food, as provided by Mielech et al. [4]

2.5 Mycotoxins

Finally, for mycotoxins, the same study provides that various excession in infant formula, infant products like cereals and nuts, were able to be detected in all countries. Apart from that, infant food and formula containing such a contaminant has had a higher average manifestation of TDI (Norway), being twice. Only products from Qatar and Poland have shown no excession in its levels in baby food and formula [4].

Type of Contamination (Number of Mycotoxins Tested)	Number of Samples	Type of Food Sample	Results	Country [Reference]
		CONTAMINANT CONTENT		
Mycotoxins	1207	[c] Infant formula, milk	Only 1% of samples exceeded the norm	China [60]
Mycotoxins (14)	215	[a] Infant food (cereal products)	Contamination of 31% of cereals, 19% of baby cereals; norms were exceeded	Brazil [51]
Mycotoxins (1: aflatoxin M1)	185	[a] Infant food (dairy products), [c] infant formula	85% of infant formula samples exceeded the MCL	Jordan [54]
Mycotoxins (5)	137	[a] Infant food (cereal and nuts products)	Contamination of 42% of baby food samples	Nigeria [56]
Mycotoxins (1: aflatoxin M1)	101	[a] Infant food (dairy products), [c] infant formula	1 sample of infant formula contaminated	Serbia [59]
Mycotoxins (1: aflatoxin M1)	84	[c] Infant formula	Contamination of 3% of samples, norms were not exceeded	Turkey [58]
Mycotoxins (1: ochratoxin A)	64	[a] Infant food (cereal products)	Contamination of 41% of cereal samples	Iran [55]
Mycotoxins (5)	60	[a] Infant food (cereal products)	Contamination of 20% of cereal samples, of which 10% exceeded maximum level	Spain [52]
		ESTIMATION OF INTAKE		
Mycotoxin (1: Deoxynivalenol)	3309	[a] Infant food, [c] infant formula, milk	Average exposure twice as high as TDI	Norway [57]
Mycotoxins (1: patulin)	610	[b] Commercial food for toddlers (apple-based products)	No exceedances of PMTDI standards	Qatar [50]
Mycotoxins (5)	302	[a] Infant food and [b] commercial food for toddlers (cereal products)	No exceedances of TDI standards	Poland [53]

Figure 11. Mycotoxin Variants Contaminant in Children Food as provided by Mielech et al. [4]

Conclusion

The composition of commercial food for children (i.e. infant, baby, toddlers) has been constantly changing throughout the years, therefore, a lot of enhancements are done due to the different studies that constantly contributes to its overall improvement by also prioritizing the safety of these target audiences. Currently, due to the fact that a lot of commercial infant and baby food are available in the market, it was found to have contained non-essential and essential elements with attributes contributing to the overall toxicological activity of the product on its consumers. In line with this, the minimization of such toxicological requirements should be prioritized; it should be that it is able to fulfill the conditions required by FDA involving quality factors for normal growth and health and the content of all nutritional ingredients in the product. This comprehensive review can help in reminding companies with the toxic elements that must be controlled and regulated and a greater data collection and exposure assessments could provide information and to help formulate risk management strategies when a certain toxicity with regards to infant food occurs. This will also be helpful for parents in choosing the right baby foods for their children to uphold the right of children to proper accumulation of health and lessened occurrence of diseases. Only through this will children be able to uphold their rights as they grow older, as they are exposed to the capacity of being provided with food containing utmostly healthy ingredients.

Recommendation

More studies should be done for the long-term effects of toxicological elements found in infant and baby food. The ultimate connection of these elements and substances to the growth of children should be studied and addressed in such a way that it would help address the toxicities as early as pre-birth. Finally, more toxicological elements found in food should also be examined to immediately address probable adverse effects through its intake.

Conflict of Interests

No conflict of interests are hereby declared by the authors.

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