Determination of Element Concentrations in Commercial Infant Formulas Using Atomic Absorption Spectrometry

Songul Unuvar^{a,*}, Ebru Kuyumcu Savan^b, and Nagihan M. Karaaslan^c

^a Inonu University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, 44280 Malatya, Turkey

^b Inonu University, Faculty of Pharmacy, Department of Analytical Chemistry, 44280 Malatya, Turkey

^c Munzur University, Faculty of Engineering, Department of Chemical Engineering, 62000 Tunceli, Turkey

INTRODUCTION

Nutrition is crucial to health and growth, particularly for infants and children (1). There are some options to breast milk which play an important role in the nutrition of infants but the World Health Organization (WHO) suggests breastfeeding as the best nutritional choice (2). The nutritional benefits of breastfeeding include protection against diseases (3-4). Nevertheless, in some cases breastfeeding has to be interrupted and the babies are fed with an infant formula or when the mothers cannot provide enough milk to meet their nutritional needs and they combine breast milk with an infant formula (5). Infant formulas are usually made from milk-based feeds; some are made from soybean which is suitable for those who are allergic to cow's milk (6). The most commonly used infant formulas contain purified cow's milk as a source of protein, with a mixture of vegetable oils as a fat source, lactose as a carbohydrate source, vitamin-mineral combinations and other ingredients depending on the manufacturer (7). In certain subpopulations, infants and small children may be at more risk when consuming contaminated foods (8). The tissue contaminant/toxin level in newborns can rise to higher levels compared to adults because of their low body weight and high food consumption per kg of body weight (9). In order to determine the safety and quality of milk and dairy products, toxic

ABSTRACT

The presence of heavy metals, inadequate minerals and elements in infant foods is of great concern. In this study, the heavy metals aluminum (Al) and lead (Pb), essential elements such as iron (Fe) and zinc (Zn), and minerals such as calcium (Ca), potassium (K), magnesium (Mg), and sodium (Na) were determined by atomic absorption spectrometry (AAS) in five different brands of 20 infant formula samples obtained from pharmacies and supermarkets in Malatya, Turkey. The Joint FAO/WHO Expert Committee on Food Additives (JECFA) has set the maximum concentration levels of heavy metals in infant formula and levels of provisional tolerable weekly intake (PTWI) of these metals by infants. The levels of Al and Pb in the analyzed samples were found to be under legal limits. The recommended daily intake (RDI) of the essential elements and minerals were found within normal and permissible ranges, showing that the formulas are safe for infants.

metal levels are important components. Symptoms of heavy metal toxicity include dizziness, nausea, vomiting, diarrhea, sleeping disorders, loss of appetite, reduced awareness and attention deficit conditions. Heavy metal toxicity is also associated with Alzheimer's disease, Parkinson's disease, autism, lupus, amyotrophic lateral sclerosis, cardiovascular disease, depressed growth, and can cause fertility problems, nervous and immune system disorders, miscarriage, and even lead to infant deaths (10). For heavy metals, any exposure is unde-

sirable, but acceptable levels have been determined for most food supplies.

Trace elements and minerals are necessary for biological processes and play an important role for normal growth and development. The rate of growth in infancy and early childhood is very high and trace element requirements are more critical during these periods. In the developing countries, inadequate complementary foods are one of the major causes of malnutrition (11). Currently, adding vitamins and trace elements to the products is a common practice among manufacturers. Sometimes, these have been added in large quantities to the point that they have been found to be toxic, even though they are essential in smaller, physiological amounts (12). For example, zinc is important for growth and muscle development of an infant and plays an important role in cell division which is massive during infancy; thus it is intentionally added to infant formulas. If too much Zn is added, it causes toxicity (13). Therefore, keeping the level of the added elements under control is necessary (14). The WHO has made suggestions as to the RDI (recommended daily intake) of minerals for infants and specified maximum levels of concentrations of toxic metals in infant formulas and levels of PTWI (provisional tolerable weekly intake) (15). Since the first year of an infant's life is very important for the development of the nervous, reproductive, digestive, respiratory and immune systems, baby food composition and consumption patterns are extremely important (16).

* Corresponding author.
E-mail: songul.unuvar@inonu.edu.tr
Tel: +90 422 341 0660
Fax: +90 422 341 1217

In the present study, the contamination levels of formulas used for infants from 0–12 months old are studied with regard to the heavy metals of Pb and Al, the essential elements Fe and Zn, and the minerals Ca, K, Mg, and Na.

EXPERIMENTAL

Instrumentation

Analysis was carried out using a PerkinElmer® AAnalyst™ 800 flame atomic absorption spectrometer (FAAS), equipped with THGA® graphite furnace, and Zeeman-effect background corrector (PerkinElmer, Inc., Shelton, CT, USA). Flame measurements were performed with a single slot burner head (10 cm for air-acetylene flame, 5 cm for nitrous oxide flame) and a lamp. Al, Ca, Fe, K, Mg, Na, and Zn were determined with FAAS and the instrument operational parameters are listed in Table I. The determination of Pb was performed by graphite furnace atomic absorption spectrometer (GFAAS) and pyrolytically coated graphite tubes (PerkinElmer part no. B3 000641) with a platform and argon was used as the inert gas. The samples were injected

into the graphite furnace using a Perkin-Elmer AS-91 autosampler (Table I). For the sample pretreatment a Milestone Start D closed vessel microwave system, operated at the maximum exit power of 1000 W was employed (Milestone Start S Microwave Labstation for Synthesis, Milestone Inc., USA). The samples were introduced inside high pressure vessels of 100-mL inner volume and nine samples were treated simultaneously. Teflon® reaction vessels were used for all digestion procedures. The reaction vessels were cleaned using 5 mL of concentrated nitric acid before each digestion.

Reagents and Standard Solutions

All chemicals were of analytical reagent grade. For the preparation of all solutions, double distilled water using a Milli-Q® system (18.2 $\mu\Omega$ cm⁻¹ resistivity, Millipore Corporation, USA) was used for all experiments. Suprapur® HNO₃ and H₂O₂ (E. Merck, Germany) were used. The element standard solutions were prepared by diluting a stock solution of 1000 mg L⁻¹ Al, Ca, Fe, K, Mg, Na, Pb, and Zn. Mg(NO₃)₂ and

Pd (Inorganic Ventures/IV Labs.) were used as the matrix modifier for lead determination. A stock solution of palladium 0.3% (m/v) and 0.5% (m/v) Mg(NO₃)₂ was prepared in 1% HNO₃. The palladium-magnesium nitrate modifier was used as a mixture of 15 μ g Pd + 50 μ g Mg(NO₃)₂ (17).

Infant Formula Preparation

Twenty infant formulas from five different manufacturers were collected from pharmacies and supermarkets in Malatya, Turkey. Each sample was labeled to identify the source, site, and date of sampling. All samples were stored paying attention to the manufacturer's instructions and sampled directly from their packaging to avoid extraneous contamination.

The infant formula samples were dried at a temperature of 105 °C for 24 hours. For microwave digestion, the samples and the standard reference material (NIST-SRM 8418 Wheat Gluten, National Institute of Standards and Technology, Gaithersburg, MD, USA.) were weighed at about 0.50 g. The samples were transferred to 100-mL Teflon® vessels. 7 mL of concentrated HNO₃ and 1 mL H₂O₂ were added and digested in the Milestone DG-FO-29 microwave oven (Milestone Start S Microwave Labstation for Synthesis, Milestone Inc., USA). The following program was run: Step 1: 10 minutes to reach 200 °C, Step 2: 20 minutes to reach 120 °C, at 1000 W, then cooled at room temperature (20 minutes). The clear solutions were transferred into volumetric flasks and diluted to 25 mL with ultrapure water. Calibrations were accomplished using direct calibration against aqueous standards. Working standard solutions were made up each day by dilution from stock standard solutions in 2% nitric acid to a final acid concentration similar to the digested samples.

TABLE I
Instrumental Operating Conditions for FAAS and GFAAS

FAAS							
Element	Acetylene	Air	Wavelength	Slit Width	Measurement Time		
	(L/min)	(L/min)	(nm)	(nm)	(sec)		
Al	2.0	17.0	309.3	0.7	3		
Ca	2.0	17.0	422.7	0.7	3		
Fe	2.0	17.0	248.3	0.2	3		
K	2.0	17.0	766.5	0.2	3		
Mg	2.0	17.0	285.2	0.7	3		
Na	2.0	17.0	589.0	0.2	3		
Zn	2.0	17.0	213.9	0.7	3		
GFAAS							
Element	Sample Volume	Modifier	Wave-length	Slit Width	Pyrolysis Temp.	Atomization Temp.	Measurement Time
	(μL)	(μL)	(nm)	(nm)	(°C)	(°C)	(sec)
Pb	10	3	283.3	0.7	1900	2450	3

Statistical Analysis

The minimum, maximum, mean, and standard deviations of the data were subjected to statistical analysis using Microsoft® Office EXCEL® software (version 2007, Microsoft Corporation, USA).

RESULTS AND DISCUSSION

The limits of detection (LOD) and limits of quantification (LOQ) were calculated from the expressions $LOD = 3SD/b$ and $LOQ = 10SD/b$, where SD is the standard deviation of the blank and b is the slope of the analytical curve. As can be seen from Table II, the limits of detection values of the AAS are adequate for the determination of the trace elements in the infant formulas. The repeatability was calculated as the relative standard deviation (RSD%). The precision of the results was satisfactory resulting in relative standard deviations varying from 0.48% to 1.17%.

The average concentrations of Al, Ca, Fe, K, Mg, Na, Pb, and Zn in infant formulas were determined with FAAS and GFAAS as shown in Table III. The average heavy metal contents in an infant formula for a

0–6 months old and a 7–12 months old were found at $1.29 \pm 0.66 \mu\text{g g}^{-1}$ for Al, $0.16 \pm 0.02 \mu\text{g g}^{-1}$ for Pb, and $1.54 \pm 0.35 \mu\text{g g}^{-1}$ for Al, and $0.18 \pm 0.08 \mu\text{g g}^{-1}$ for Pb, respectively. The average essential element contents in an infant formula for a 0–6 months old infant and a 7–12 months old infant were found at $61.34 \pm 13.72 \mu\text{g g}^{-1}$ for Fe, $29.72 \pm 4.04 \mu\text{g g}^{-1}$ for Zn, $72.6 \pm 4.05 \mu\text{g g}^{-1}$ for Fe, and $34.64 \pm 6.32 \mu\text{g g}^{-1}$ for Zn, respectively. The average mineral contents in a 0–6 month infant formula were found at $4.19 \pm 0.45 \text{ mg g}^{-1}$ for Ca, $6.53 \pm 1.09 \text{ mg g}^{-1}$ for K, $0.51 \pm 0.08 \text{ mg g}^{-1}$ for Mg, $0.95 \pm 0.19 \text{ mg g}^{-1}$ for Na, and for a 7–12 month infant formula were $4.35 \pm 0.96 \text{ mg g}^{-1}$ for Ca, $6.08 \pm 2.27 \text{ mg g}^{-1}$ for K, $0.50 \pm 0.15 \text{ mg g}^{-1}$ for Mg, and $1.89 \pm 0.75 \text{ mg g}^{-1}$ for Na, respectively. None of the samples contained aluminum or lead in amounts that could repre-

sent a health hazard for infants. All concentrations of essential elements and minerals were found within the recommended values.

The accuracy of the results was verified by analyzing the concentration of Al, Ca, Fe, K, Mg, Na, Pb, and Zn in NIST-SRM 8418 Wheat Gluten. The certified and observed values for the NIST-SRM 8418 Wheat Gluten are presented in Table IV. The results of the analyzed metals were generally in agreement with the NIST certified values. The obtained recoveries of the standard reference material NIST-SRM 8418 Wheat Gluten were 92% for Al, 87% for Ca, 93% for Fe, 89% for K, 97% for Mg, 96% for Na, 90% for Pb, and 91% for Zn.

The mean daily intake of the elements was calculated based on the estimated average amount of infant formulae (g day^{-1}). The recommended daily intake (RDI) is the average daily dietary intake level that is sufficient to meet the nutrient requirements of nearly all (97 to 98%) individuals in a life stage and gender group (18). The daily intake of Al, Ca, Fe, K, Mg, Na, Pb, and Zn was analyzed and calculated and the results are listed in Table V.

TABLE II
Detection Limits ($\mu\text{g g}^{-1}$),
($N^a=10$)

Element	RSD ^b (%)	LOD	LOQ
Al	0.77	1.90	6.35
Ca	0.84	0.79	2.64
Fe	0.61	0.33	1.12
K	0.6	0.81	2.7
Mg	0.67	0.07	0.24
Na	0.57	0.06	0.18
Pb	0.48	0.01	0.02
Zn	0.63	0.16	0.53

^a Number of determinations.

^b The relative standard deviations were calculated as percentage corresponding to $(s/x \text{ mean}) \times 100$ for blank samples.

TABLE III
Heavy and Essential
Element Concentrations
in Infant Formula Samples
Determined by AAS

(Mean $\pm$ Standard deviation, average of three repeated measurements)

Element	0–6 months (n: 10)	7–12 months (n: 10)
Al ($\mu\text{g g}^{-1}$)	1.29 ± 0.66	1.54 ± 0.35
Ca (mg g^{-1})	4.19 ± 0.45	4.35 ± 0.96
Fe ($\mu\text{g g}^{-1}$)	61.34 ± 13.72	72.6 ± 4.05
K (mg g^{-1})	6.53 ± 1.09	6.08 ± 2.27
Mg (mg g^{-1})	0.51 ± 0.08	0.50 ± 0.15
Na (mg g^{-1})	0.95 ± 0.19	1.89 ± 0.75
Pb ($\mu\text{g g}^{-1}$)	0.16 ± 0.02	0.18 ± 0.08
Zn ($\mu\text{g g}^{-1}$)	29.72 ± 4.04	34.64 ± 6.32

n=10, different samples.

TABLE IV
Results for NIST-SRM 8418
Wheat Gluten

(Mean $\pm$ Standard Deviation, average of three repeated measurements)

Elements	Certified ($\mu\text{g g}^{-1}$)	Measured ($\mu\text{g g}^{-1}$)	Recovery (%)
Al	10.8	9.9 ± 0.48	92
Ca	369	321 ± 52	87
Fe	54.3	50.5 ± 6.4	93
K	472	420 ± 61	89
Mg	510	493 ± 38	97
Na	0.142	0.136 ± 0.06	96
Pb	0.10	0.09 ± 0.01	90
Zn	53.8	48.8 ± 5.4	91

The recommended daily intake and the provisional tolerable weekly intake were calculated according to a feeding table for normal healthy babies and are listed in Tables VI and VII, respectively. The related results are presented in Table V and compared with the daily intake values recommended by WHO (15). Daily consumed powder formula values were obtained from feeding tables and the reference mean body weights were used (18). The percentages of daily intake of minerals are presented in Table VI and compared to the recommended daily intake as suggested by WHO (15).

Ca in Infant Formula

In the first year of life, human milk and infant formulas are the main sources of Ca. Even a very low Ca intake may contribute to the development of rickets in infants and children. Maintenance of adequate Ca intake during childhood is essential for the development of maximal peak bone mass. Increasing peak bone mass can be

an important way to reduce the risk of osteoporosis in adulthood (19).

Fe in Infant Formula

Fe deficiency-anemia is widely observed in premature infants and between 6 months to 2 years of age (20). Formulas without supplemental Fe have been shown to cause iron deficiency after 4 months of life. Therefore, formulas should be supplemented with Fe (21). On the other hand, Fe causes tissue damage and some other diseases in humans at high concentrations (22).

K in Infant Formula

K is a necessary mineral and an electrolyte for cardiac and tissue health, skeletal contraction and gastrointestinal function (23).

Mg in Infant Formula

Mg is widely distributed in nature and deficiency of this mineral is rare (24).

Na in Infant Formula

Na intake should vigilantly be monitored in infants since their excretory system eliminates sodium with less efficiency than in adults. Accordingly, high amounts of Na can cause immediate health implications for the young infants, besides affecting their long-term health status (23).

Zn in Infant Formula

Intake of high or low amounts of Zn can affect the health of an infant. Zn deficiency in children is characterized mainly by dermatitis and alopecia during infancy and by short stature during childhood (20).

The concentration of essential elements in the present study was therefore similar to those found in Norway (11). Zand et al. (2011) experimentally determined the values of minerals and trace elements in infant foods (except for potassium) and found that they were higher than the declared values by WHO (25).

TABLE V
Calculation of Daily Intake of Determinated Elements in Infant Formulas

Age	Reference Body Weight (kg)	Daily Consumed Powder Formula (g)	Al ^a	Ca ^b	Fe ^a	K ^b	Mg ^b	Na ^b	Pb ^a	Zn ^a
0-6 months	7	105	19.4	62.9	920.1	97.9	7.7	14.3	2.4	445.8
7-12 months	9	135	23.1	65.3	1089	91.2	7.5	28.4	2.7	519.6

^a ($\mu\text{g kg}^{-1} \text{ bw day}^{-1}$).

^b ($\text{mg kg}^{-1} \text{ bw day}^{-1}$).

TABLE VI
Comparison of Recommended Daily Intake (RDI) Value of Elements With the Calculated Daily Intake From the Menu in Table V

Element (mg)	RDI (0-6 months)	RDI (%)	RDI (7-12 months)	RDI (%)
Ca	525	11.9	525	12.4
Fe	11	8.4	11	9.9
K	800	12.2	700	13
Mg	60	12.8	75	10
Na	280	5.1	350	8.1
Zn	4	11.1	5	10.4

TABLE VII
Percentage of Provisional Tolerable Weekly Intake (PTWI) of Determined Heavy Metals

Heavy Metals ($\mu\text{g kg}^{-1} \text{ bw week}^{-1}$)	PTWI ($\mu\text{g kg}^{-1} \text{ bw week}^{-1}$)	0-6 mo. PTWI (%)	7-12 mo. PTWI (%)
Al	2000	135.8	6.79
Pb	25	16.8	67.2

Pb and Al in Infant Formula

Table VII shows the weekly Pb and Al intake and (%) of provisional tolerable weekly intake (PTWI) calculated according to Table V. Aluminum is not considered to be an essential element for infants but excessive amounts cause an increased deposition of Al in the bone and in the central nervous system, thus causing reduced renal function in infants and children. In addition, increased amounts of dietary Al may contribute to decreased skeletal mineralization (26, 27). Aluminum compounds are used as food additives in foods in some countries (28). Many of the formulas were packaged using aluminum-based materials. The content of Al both in ready-to-drink milks and milk powders has been reported by Chuchu et al. (2013) to be higher than permissible limits (29). The mean values for Al in formulas of the present study do not exceed the JECFA (Joint Expert Committee for Food Additives) established PTWI of 2000 $\mu\text{g/kg}$ bw/week (30) and are similar to those found in a Canadian study (31). Therefore, the control of Al in infant formulas seems to be essential. Infants and young children may absorb as much as 50% of dietary Pb, compared to only 10% for adults (32). As a result of its natural presence in the environment, Pb also occurs naturally at low levels in the food chain and in commercial food products. While Pb can be harmful to the health of people of all ages, infants and children are a susceptible subpopulation for Pb exposure. This age group is particularly at risk of the neurodevelopmental effects of Pb exposure, resulting in the reduction of the Intelligence Quotient (IQ) score and attention-related behaviors (attention-deficit hyperactivity disorder) (33). In addition, high levels of Pb in the body cause anemia, colic, headache, brain damage, and central nervous system

disorder (22). The FAO/WHO JECFA set the PTWI for lead at 25 $\mu\text{g kg}^{-1}$ bw/week¹ for infants (34, 35). Thus regular monitoring of heavy metals such as lead in infant foods is most important (32).

The most ideal way of feeding babies is breastfeeding. As well as protecting babies against infection, breastfeeding prevents the progress of allergic diseases (9). However, WHO reports that only 38% of infants receive breast milk in their first 6 months worldwide (15). From the results of some studies, it is evident that the infant formula samples were contaminated with variable amounts of heavy metals (4, 6, 8-10, 12-14, 29, 31, 32, 36). The effect of metal poisoning in infants is compounded by the fact that even at low levels of exposure, metals bioaccumulate in the vital organs such as the kidneys, an effect that persists in adulthood (36). Due to the bioaccumulation of metals, the presence of toxic metals in infant foods is of great concern and therefore, infant formula products need regular monitoring to ascertain infant safety. In this study, it was found that the minerals determined in the studied infant formula samples do not fall below the recommended daily intake and the toxic metal levels were within the acceptable/standard limits and were not observed to cause any significant toxicity.

CONCLUSION

In the present study, the contents of heavy metals, essential elements and minerals (Al, Ca, Fe, Mg, Na, K, Pb, and Zn) in different infant formulas were investigated. For this aim, 20 infant formulas from five different manufacturers were collected from pharmacies and supermarkets in Malatya, Turkey and analyzed by atomic absorption spectrometry. The obtained results showed that none of the samples contained Al or Pb

in amounts that could represent a health hazard for infants. In addition, all concentrations of the essential elements and minerals were also found within the recommended FAO/WHO values. This study demonstrated that continued investigation about the element composition in infant formulas is essential and needed.

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REFERENCES

1. J. Cross, *Newborn and Infant Nursing Reviews* 15,128 (2015).
2. WHO, *Strengthening action to improve feeding of infants and young children 6-23 months of age in nutrition and child health programmer*. Geneva, Switzerland, (6-9 Oct. 2008).
3. W.H. Oddy, *Breastfeeding Rev.* J. 9, 8 (2001).
4. O.R. Johnson and O.O. Samson, *Scholars Academ. J. Biosci.* 1, 318 (2013).
5. C. Sabater, M. Prodanov, A. Olano, N. Corzo and A. Montilla, *Food Chem.* 194, 6 (2016).
6. S.A.M. Burrell and C. Exley, *BMC Pediatric.* 10, 63 (2010).
7. A. Ryan, *Pediatric.* 99, 12 (1997).
8. G.R.J. Khaniki, *Int. J. Dairy Tech.* 2, 104 (2007).
9. A. Oskarsson, I. Palminger and J.P.K. Sundberg, *Analyst* 123, 19 (1998).
10. S.F.A. Abd-El Aal, *J. Americ. Sci.* 8, 665 (2012).
11. R. Melo, K. Gellein, L., Evje and T. Syversen, *Food Chem. Toxicol.* 46, 3339 (2008).
12. G. Lutfullah, A.A. Khan, A.Y. Amjad and S. Perveen, *Sci. World J.* 1 (2014).
13. V.O. Odhiambo, *MSc Thesis, Kenyatta University, Nairobi, Kenya* (2014).
14. F.A.A.E. Salah, I.A. Esmat and A.B. Mohamed, *Int. Food Res. J.* 20, 1807 (2013).
15. WHO, *Complementary feeding.*

- Infant and Young Child Feeding: Model Chapter for Textbooks for Medical Students and Allied Health Professionals, 7,19 (2009).
16. M. Pandelova, W.L. Lopez, B. Michalke and K.W. Schramm, J. Food Comp. Anal. 27, 120 (2012).
  17. P.Vim, D.L. Massart, and J. Smeyers-Verbeke, Fresenius J. Anal. Chem. 343, 526 (1992).
  18. Food and Nutrition Board, Institute Of Medicine. Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride. Washington, DC: The National Academies Press (USA). (1997).
  19. S.S. Baker, W.J. Cochran, C.A. Flores, M.K Georgieff, M.S Jacobson, T. Jaksic and N.F. Krebs, Pediatrics 104, 1152 (1999).
  20. H. Kodama, Japan Medic. Assoc. 47, 376 (2004).
  21. B. Lonnerdal, J. Nut. 119, 1839 (1989).
  22. A. Shah, A. Niaz, N. Ullah, A. Rehman, M. Akhlaq, M. Zakir and M.S. Khan, J. of Chem. 1 (2013).
  23. A. Waseem, M. Nafees, G. Murtaza, A. Sajjad, Z. Mehmood, and A.R. Siddiqi, Iran. J. Public Health 43, 1204 (2014).
  24. Committee on the Evaluation of the Addition of Ingredients New to Infant. Comparing Infant Formulas with Human Milk, Washington, D.C.: National Academies Press (USA), (2004).
  25. N. Zand, B.Z. Chowdhry, F.B. Zotor, D.S. Wray, P. Amuna and F.S. Pullen, Food Chem. 128, 123 (2011).
  26. F.R. De Amorim, C. Bof, M.B. Franco, J.B.B. Da Silva and C.C. Nascentes, Microchem. J.82, 168 (2006).
  27. J. Bhatia and F. Greer, Pediatric. 12, 1062 (2008).
  28. M.G. Soni, S.M. White, W.G. Flamm and G.A. Burdock, Regul. Toxic. Pharm. 33, 66 (2001).
  29. N. Chuchu, B. Patel, B. Sebastian and C. Exley, BMC Pediatric. 13, 162 (2013).
  30. J.E.C.F.A. Seventy-fourth Meeting of the Joint FAO/WHO Expert Committee on Food Additives (2011).
  31. R. Dabeka, A. Fouquet, S. Belisle and S. Turcotte, Food Add. & Contam., Part A, Chem. Anal. Cont. Exposure & Risk Assess. 28, 744 (2011).
  32. L.M. Hafez and A.M. Kishk, The J. Eryp. Pub. Health Assoc. 83, 3 (2008).
  33. Environment Canada, Health Canada. Risk Management Strategy for Canada (2010).
  34. FAO/WHO, Evaluation of certain food additives and contaminants. Fifty-seventh report of the Joint FAO/WHO Expert Committee on Food Additives, Vol. 909 (2002).
  35. FAO/WHO, Evaluation of certain food additives. Seventy-first report of the Joint FAO/WHO Expert Committee on Food Additives, Vol. 956 (2010).
  36. V.O. Odhiambo, R. Wanjau, J.O. Odundo and M.P. Nawiri, Afr. J. Food Sci. 9, 437 (2015).