Chapter

The Evaluation of Childhood Foods and Infant Formula Exposure to Furan, Chloropropanols and Acrylamide Contamination by Food Processing

Burhan Başaran

Abstract

This review attempted to evaluate the exposure of thermal processing contaminants such as furan, chloropropanols and acrylamide from infant formulas. Furan, chloropropanols and acrylamide exist at varying levels in several types of foods that are consumed in daily diet including infant formulas. The consumption of these foods leads to the exposure to the thermal processing contaminants. In this sense, it is apparent that humans face hidden danger through dietary exposure throughout their lives. Infants are considered as the age group that expose to the highest levels of these substances as a result of the fact that they have low body weight and consume infant formulas in their diets as alternative nutrition. The review emphasizes that the infant formulas are not innocent, on the contrary, they can be considered as safety critical for infants considering that infant formulas include furan, chloropropanols and acrylamide. Therefore, this review suggests that in this sense all shareholders' (university, non-governmental organizations, public and private sector) acting in concert with each other is crucially important for the health of individuals and overall society.

Keywords: infant formulas, furan, chloropropanols, 3-MCPD, 2-MCPD, glycidol, acrylamide, exposure

1. Introduction

World Health Organization (WHO) and UNICEF advices that infants need to be exclusively breasted for the first 6 months and breastfeeding should last minimum 2 years. Nevertheless, around the world, the rate of breastfeeding in the first 6 months is still 38% and this percentage has not changed for about 20 years. It is known that breast milk significantly contributes to infants' physical and mental development and acts as a protector for infants against several diseases. Therefore, with the contributions of WHO and UNICEF, breast milk is being promoted in order to increase the rate of breastfeeding to 50% for the first 6 months until 2025 and studies are being carried out with regard to the importance of breast feeding in early periods of infancy [1, 2].

Use of breast feeding as primary nutrition in early periods, namely in the first 6 months, of infancy is highly common around the world (Norway: 95%, Australia: 92%, Canada: 89%, United States: 77%) and the percentage increases gradually year by year. On the contrary, after 6 months is decreasing dramatically [3]. By all means, there are several factors affecting this case. Some of these factors are mothers' becoming a mother young, not having breastfeeding experience, concern of insufficient breast milk, desire to feed their babies with new tastes, active work life, long working hours and perceptions of mothers created by other individuals, mother's and baby's health condition, babies' becoming acquainted with pacifier and feeding bottle [4–6]. Besides these factors, depending on the development of the baby, mothers generally give their babies other nourishments as supplement to breast milk or use them as only source of nutrition for their babies. The top of these nourishments is infant formulas.

There are several firms operating globally in the sector of infant formulas which has become a massive market today. These firms invest in research-development activities, advertising activities and develop marketing strategies in order to gain advantage in the competition [7]. It is easy to find several follow-on milk, follow-on formulas and mixed formulas for the needs of 0–6 months-old and >6 months-old babies, which are formulated either in powder or liquid form and enriched with various ingredients [8]. Infant formulas are often preferred in that they are accessible and easy to prepare; besides, they can be used by others when mother is not available for feeding. On the other hand, it is known that mothers are deeply anxious about the infant formulas although they try to make their best to choose the most appropriate formula for their babies based on their research on written and visual media, advices from others and past experiences [9, 10].

On one hand, it is beyond argument that breast milk is the best choice for babies' nourishment, development and health; on the other hand, it is not always the one and only choice because of various reasons. Therefore, it needs to be ensured that the adverse effects of infant formulas, which are used as supplement to breast milk or used exclusively, on babies' health in the short-, medium- and long-term are eliminated and these formulas not to cause any health problems for babies. In this respect, certain legal regulations are designed for the production and marketing of infant formulas nationally and globally. However, in the literature, although infant formulas carry the risk with respect to furan, acrylamide, chloropropanols and polycyclic aromatic hydrocarbons, which are called thermal processing contaminants and have potential to cause various health problems for humans, this information has not been referred in the legal regulations. Considering that the contaminants in question are included in various foods that are frequently preferred in daily diets, individuals expose to these contaminants starting from very early periods of infancy and this exposure continues throughout their lives. To this end, the current review aims to evaluate the infant formulas with respect to certain thermal processing contaminants.

2. Thermal process contaminants

Besides bringing certain sensorial properties to foods, thermal process is a processing technique that eliminates or decreases the potential hazards originating from foods against consumers' health through making foods microbiologically more reliable. However, under certain conditions thermal processing applications cause certain toxic substances called "thermal processing contaminants" (heterocyclic aromatic amines, 5-hydroxymethylfurfural, polycyclic aromatic hydrocarbons, nitrosamines, furan, acrylamide, and chloropropanols) to emerge [11, 12]. In the last 10 years, a great amount of research has focused on thermal processing contaminants and this topic is still current and important for consumers, health authorities and industries [13].

2.1 Furan

Furan is colorless, highly volatile and flammable compound with a boiling point close to room temperature (≈31°C). It is soluble in most of the organic solvents such as alcohol and acetone. Furan with a molecular formula of C_4H_4O and CAS number of 110-00-9 is a heterocyclic and aromatic compound [14].

Formation of furan in foods is the result of various mechanisms. It has been documented that besides the presence of reducing sugar or amino acids, thermal degradation or Maillard reaction, ascorbic acid, thermal oxidation, oxidized polyunsaturated lipids, serine and cysteine without other sources [15, 16].

In the risk assessment undertaken by U.S. National Institutes of Health (NIH) and Joint FAO/WHO Expert Committee on Food Additives (JECFA) depending on the studies on laboratory animals, furan was reported to be a strong carcinogenic compound that affected several organs [17, 18]. It has been identified as "possibly carcinogen to humans" (Group 2B) by International Agency for Research on Cancer (IARC) [19].

In a study conducted by The US Food and Drug Administration (FDA) in year 2004 with 334 foodstuffs, presence of furan was reported for canned and jarred baby foods, infant formulas, coffees, meats, fish, soups, sauces, vegetables and fruits and several other foodstuffs that underwent thermal processing. Particularly, the study reported that all baby foods included furan [20]. After FD reports, The European Commission Recommendation 2007/196/EC offered a suggestion to the member countries in order for tracking the toxicity, formation, analysis and the exposure of furan [21]. Based on the reports from several countries, JECFA reported the foodstuffs that included the highest furan levels; roasted coffee (powder) (814–4590 μg/kg), instant coffee (powder) (90–783 μg/kg), brewed roasted coffee (34–113 μg/kg), baby food (19–96 μg/kg), soya sauce (16–52 μg/kg), canned fish (6–76 μg/kg) and baked beans (27–581 μg/kg) [22]. According to the reports of European Food Safety Authority (EFSA) and FDA, Crews and Castle classified the foodstuffs in three categories that included furan more than 100 μg/kg; coffee, baby foods, sauces and soups. Moreover, furan was found in 262 of 273 baby foods, 70 of 71 infant foods, 28 of 42 infant formulas. The levels of furan in baby foods, infant foods and infant formulas change between the ranges of 1–112 μg/kg (mean: 28 μg/kg), 1.3–87.3 μg/kg (mean: 27 μg/kg) and 2.5–27 μg/kg (mean: 12 μg/kg), respectively [23]. Several studies reported different levels of furan in baby foods and infant formulas; EFSA 31–32, 0.2–3.2 μg/kg, Liu and Tsai 4.23–124.1, 2.4–28.7 μg/kg [24, 25]. Lambert et al. determined the furan levels of many foods including baby foods and infant formulas (**Table 1**) [26].

In this respect, **Table 2** displays the results of dietary exposure of furan in individuals from diverse group of ages reported by EFSA.

The mean of infants' dietary exposure of furan was reported as 0.99–1.34 μg/kg bw per day by FAO/WHO whereas Health Canada reported this level as 1.76 μg/kg bw per day [17, 28]. Some studies reported the mean of dietary exposure of furan for 4 months, 5–6 months, 7–12 months and 13–36 months old infants as 0.14, 0.60, 0.84 and 0.37 μg/kg bw per day [29] and 0.09, 0.56, 0.80 and 0.33 μg/kg bw per day, respectively [30].

Food group	Mean (µg/kg)
Baby foods	3.3–41
Infant formulae	3.5–5.7
Vegetables	5.9–6.3
Fish	5.3–5.3
Cereal products	44–44
Meat products	7.3–7.5
Milk products	1.4–2.3
Soups	16–16

*The data were taken directly from Lambert et al.

Table 1.
The mean level of furan in different food groups [26].

Age group	Mean dietary exposure (µg/kg bw per day)	High dietary exposure (µg/kg bw per day)
Infants	0.14–0.99	0.27–1.82
Toddlers	0.22–0.65	0.05–0.31
Other children	0.19–0.52	0.29–0.86
Adolescents	0.11–0.54	0.20–1.22
Adults	0.03–0.59	0.08–1.29
Elderly	0.12–0.61	0.24–1.27
Very elderly	0.13–0.75	0.27–0.96

*The data were taken directly from EFSA Journal.

Table 2.
Dietary exposure of furan [27].

2.2 Chloropropanols

In recent years, the presence of chloropropanols (certain fatty acid esters of 3-monochloro-1,2-propanediol (3-MCPD) and the related substance glycidol, 2-monochloro-1,3-propanediol (2-MCPD), 1,3-dichloro-2-propanol (1,3-DCP) and 2,3-dichloro-1-propanol (2,3-DCP)) in foodstuffs has aroused the attention of researchers [31]. Dichloropropanols are comprised of monoesters whereas monochloropropanediols are comprised of both monoesters and diesters [32]. It has been estimated that depending on thermal processing, lipids, glycerol, triolein and lecithin that are heated with hydrochloric acid are precursors in the formation of chloropropanols in foodstuffs [33, 34]. Chloropropanols and its esters are created from lipids and chlorides in the oil refining process particularly when the deodorization process is realized under high temperatures. Moreover, glycidol can occur through dehalogenation from 3-MCPD [35].

It has not been ascertained that whether chloropropanol is a carcinogenic compound. On the other hand, it is disturbing that some free chloropropanol forms in foodstuffs are potentially toxic. The JECFA reported that 1,3-DCP is a genotoxic carcinogen, however, there is not enough evidence for the toxicologic evaluation of 2-MCPD [36, 37]. In this respect, Lee and Khor found that 3-MCPD and 1,3-DCP have potential genotoxic and carcinogenic characteristics [38]. Similarly, Onami et al. suggested that 3-MCPD carries unignorable risks for human health with regard to its potential hazard [39]. In some other studies 1,3-DCP and 3-MCPD are defined as possible human carcinogens (group 2B) and similarly glycidol is referred as a probable human carcinogen (group 2A) [40–42]. One of the most comprehensive studies on the toxicologic evaluation of chloropropanols revealed that whereas the carcinogenic effect of 1,3-DCP was highly evident, for the reason that the level of its presence in foodstuffs was considerably low, 1,3-DCP did not carry a risk for human health. This comprehensive study emphasized the insufficiency of the research on the level of the presence of 2-MCPD and 2,3-DCP in foodstuffs and the toxicologic evaluation of these substances. However, current evidence suggests that these compounds can be considered within low risk group for human health for the reason that the level of the presence of these compounds in foodstuffs is low [43]. EFSA determined the tolerable daily intake (TDI) for 3-MCPD as 0.8 μg/kg bw per day, whereas JECFA suggested the provisional maximum tolerable daily intake (PMTDI) of 4 μg/kg bw/day [44, 45].

Recent studies revealed that chloropropanols was found in several foodstuffs at different levels particularly in soy sauces, meat and meat products, fish and sea foods, cereals, snacks, bread, biscuits, crisps, chips, baby foods and infant formulas as well [46, 47]. **Table 3** shows the levels of chloropropanols in foodstuffs reported in the comprehensive study by EFSA.

Considering the other studies on infant formulas and chloropropanols, Zelinková et al. identified 3-MCPD as 1.04–2.03 mg/kg, Weißhaar identified glycidol as 2.6–5.3 mg/kg, and Wöhrlin et al. identified 3-MCPD as 0.42 mg/kg and 2-MCPD, 0.19 mg/kg, glycidol 0.36 mg/kg [49–51]. **Table 4** displays the results suggested by EFSA regarding the dietary exposure of chloropropanols for the individuals from different age groups.

EFSA revealed that the food group that contributes 50% and higher levels of 3-MCPD, 2-MCPD and glycidol exposure for infants is infant formulas and follow-on formulas, which are followed by vegetable fats and oils, besides cookies. The levels of 3-MCPD, 2-MCPD and glycidol considering the exposure from only infant formulas were calculated as 2.4, 0.7–1.3, and 1.8–2.1 μg/kg bw per day, respectively [48]. JECFA estimated the average exposure to glycidol equivalents for babies between 0.1 and 3.6 μg/kg bw/day. However, the exposure level of 3-MCPD equivalents can increase to 10 μg/kg bw/day on average for the babies that are fed by infant formulas in the early periods of their lives [45]. Spungen et al. estimated the exposure of 3-MCPD equivalents for 0–1, 2–3 and 5–6 months old babies as 10,

Food groups	3-MCPD μg/kg	2-MCPD μg/kg	Glycidol μg/kg
Vegetable fats and oils	1093 (1090–1095)	414 (400–427)	1268 (1259–1277)
Margarine and similar products	408 (406–409)	159 (152–166)	361 (358–364)
Infant formulas (powder)	108 (108–109)	44 (31–58)	87 (80–94)
Cereal-based products and similar	83 (77–90)	42 (38–47)	51 (50–51)
Fried, baked or roast meat or fish products	30 (26–34)	10 (7–14)	38 (38–39)
Smoked meat or fish products	21 (15–28)	6.2 (0.5–11)	17 (15–19)
Snacks and potato products	130 (123–137)	79 (75–84)	58 (58–59)

The data were taken directly from EFSA Journal.

Table 3.
The mean level of 3-MCPD, 2-MCPD, glycidol and esters in different food groups [48].

Age group	3-MCPD μg/kg bw per day	2-MCPD μg/kg bw per day	Glycidol μg/kg bw per day
Infants	0.5–1.0	0.2–0.4	0.4–0.8
Toddlers	0.6–1.4	0.3–0.6	0.4–0.9
Other children	0.5–1.5	0.3–0.7	0.3–0.9
Adolescents	0.2–0.7	0.1–0.3	0.2–0.5
Adults	0.2–0.4	0.1–0.2	0.2–0.3
Elderly	0.2–0.4	0.1–0.2	0.1–0.3
Very elderly	0.2–0.5	0.1–0.2	0.1–0.3

The data were taken directly from EFSA Journal.

Table 4.
The mean of the dietary exposure to 3-MCPD, 2-MCPD and Glycidol [48].

8, 7 μg/kg bw per day respectively, whereas the exposure of glycidol and esters were estimated 2 μg/kg bw per day and same for all age groups [52]. Arisseto et al. identified the exposure of 3-MCPD for.

0–5, 6–11 months old babies as 2.49, 1.05 μg/kg bw/day, respectively and the glycidol exposure as 3.65, 1.64 μg/kg bw/day [53].

2.3 Acrylamide

Acrylamide (AA), which was identified for the first time as a chemical compound in 1893 in Germany, is a chemical agent used extensively in such sectors as dams, tunnels, water treatment, paper and textile [54]. The presence of AA in foods for the first time was identified in 2002 by a group of researchers in Sweden [55]. Acrylamide formation in foods is explained through several mechanisms. The most important of all these mechanisms is especially Maillard reaction, which is performed in thermal processing with the presence of asparagines amino acid and reducing sugar [56]. It has been revealed that, apart from this mechanism, acrolein, B-alanine, aspartic acid, pyruvic acid and carnosine cause AA formation through various reactions [57].

In the experimental studies carried out with animals, a positive dose-response relationship between AA and the cancer in multi-organs and tissues was found [58, 59]. In epidemiological studies conducted with humans, it was suggested that AA could seriously affect fetal development [60] and neurological changes [61]. On the other hand, there is not a clear consensus on the relationship between AA and cancer yet. Whereas, some studies reveal that AA increases the risk of contracting ovarian cancer [62], lung cancer [63] and the cancers related to digestive and respiratory systems [64], some other studies determine that AA has no positive relationship with several types of cancer [65–67]. However, IARC classifies AA as a probable human carcinogen (group 2A) [68].

EFSA reported the results of the study that show AA levels in several foodstuffs in 2015 (**Table 5**).

In the other studies on infant formulas, different acrylamide levels were reported; Fohgelberg et al. found 3.5–223 μg/kg and Elias et al. found <LOD (limit of detection)-353 μg/kg [70, 71]. Likewise, **Table 6** displays the results of dietary AA exposure of the individuals from different age groups reported by EFSA.

Mojska et al. calculated the daily dietary intake of acrylamide for 6, 7, 8, 9 and 10–12 months old babies as 17.46, 20.87, 21.65, 29.06 and 38.05 μg/person/day, respectively [72]. Considering the other studies on AA exposure, Health Canada estimated the AA exposure for <1 years and 1–3 years old babies as

Food groups	Mean (μg/kg)
Potato fried products (except potato crisps and snacks)	308 (303–313)
Potato crisps and snacks	389 (388–389)
Soft bread	42 (36–49)
Breakfast cereals	161 (157–164)
Biscuits, crackers, crisp bread and similar	265 (261–269)
Coffee (dry)	522 (521–523)
Coffee substitutes (dry)	1499
Baby foods, other than cereal-based	24 (17–31)
Processed cereal-based baby foods	73 (70–76)
Other products based on potatoes, cereals and cocoa	97 (92–101)

*The data were taken directly from EFSA Journal.

Table 5.
AA the mean levels of several foods (μg/kg) [69].

Age group	Mean dietary exposure (μg/kg bw per day)	High dietary exposure (μg/kg bw per day)
Infants	0.5–1.6	1.4–2.5
Toddlers	0.9–1.9	1.4–3.4
Other children	0.9–1.6	1.4–3.2
Adolescents	0.4–0.9	0.9–2.0
Adults	0.4–0.6	0.8–1.3
Elderly	0.4–0.5	0.7–1.0
Very elderly	0.4–0.5	0.6–1.0

*The data were taken directly from EFSA Journal.

Table 6.
The mean of the dietary AA exposure [69].

0.211, 0.609 μg/kg bw per day, respectively, and Sirot et al. found the AA exposure levels for 1–4, 5–6, 7–12 and 13–36 months-old babies as 0.14, 0.03, 0.40 and 0.07 μg/kg bw per day, respectively [30, 73].

3. Acrylamide, furan and chloropropanol exposure caused by breast milk

It is estimated that babies are exposed to contaminants coming from breast milk from the first seconds of their lives. This exposure varies depending on the impact of many factors such as the age of the mother, dietary habits, living space, and environmental contaminants etc. on the compounds in breast milk. Therefore, breast milk is globally monitored as a biomarker for exposure and sheds light on exposure evaluation studies [74, 75].

The number of studies on the acrylamide level of breast milk is very limited. Sörgel et al. detected acrylamide in milk of mothers consuming foods that contain high levels of acrylamide such as potato chips, French fries etc. They stated that 10 to 50% of acrylamide occurring in pregnant women due to nutrition is transferred to the fetus through blood and it can reach µg/L in breast milk. They state that acrylamide exposure caused by breast milk continues until the end of breastfeeding, and therefore nursing mothers should avoid foods containing acrylamide until uncertainties about acrylamide are eliminated [76]. Fohgelberg et al. stated that traces of acrylamide were detected in all breast milk samples, the acrylamide level was determined as 0.51 µg/kg only in one sample while the acrylamide levels in the other 18 samples were under the limit of quantification (0.5 µg/kg). The mean acrylamide level in breast milk was assumed to be 0.25 µg/kg in the study and the mean acrylamide exposure was estimated as 0.04 µg/kg bw per day (the mean body weight is calculated as 5.5 kg) for infants that are fed only with breast milk during the early breastfeeding period. The results revealed the importance of breastfeeding as a way of preventing the baby from being exposed to acrylamide as the level of acrylamide in breast milk is very low [70].

The source and possible consequences of 3-MCPD in breast milk have not been entirely explored yet. However, it has been stated that dietary habits of mothers are an important factor for presence of 3-MCPD in breast milk [34, 77]. Zelinkova et al. determined the 3-MCPD level between 11 and 76 µg/kg and the mean amount as 35.5 µg/kg in 12 breast milk samples. They determined the 3-MCPD exposure caused by breast milk in babies (breastfed for up to 4 months) as 26,625 µg/day (average daily intake of mother's milk by the baby is about 750 mL) and 8.19 µg/kg bw per day [77]. Jędrkiewicz et al. stated that 2-MCPD and 3-MCPD reached 2.2 mg/kg in breast milk and therefore it was highly difficult for babies to avoid chloropropanols [78].

Polychlorinated dibenzofurans (PCDFs), which are another contaminant in breast milk, have been examined in studies together with polychlorinated biphenyls (PCBs) and polychlorinated dibenzo-p-dioxins (PCDDs). A lot of studies can be found in the literature on this subject compared to acrylamide and chloropropanols. As breast milk is the first and most important way of conveying PCBs and PCDD/Fs to babies, WHO has been conducting global studies on dioxin detection in breast milk since 1987 [79]. Costopoulou et al. reported that the countries with the highest level of PCBs and PCDD/Fs in breast milk are Egypt, the Netherlands, Belgium, Luxemburg, and Italy {respectively, 22.3, 18.27, 16.92, 14.97, 12.66 pg/g [fat WHO-TEQ (toxicity equivalent)]} while the countries with the lowest levels are Fiji, Brazil, the Philippines, Australia, and Bulgaria (respectively 3.34, 3.92, 3.94, 5.57 and 6.14 pg/g fat WHO-TEQ) [80]. WHO has estimated the range of tolerable daily dose as 1–4 pg TEQ/kg bs per day for babies exposed to dioxin contaminants such as PCDD/Fs and PCBs [81]. Focant et al. calculated the average concentration for total TEQ (PCDD/Fs and PCBs) as 17.81 pg/g and the daily intake of PCDD/Fs and PCBs as 62.3 TEQ/kg bw per day [82]. In a study they conducted in China (Guangdong Province), Huang et al. predicted the mean EDI level of PCDD/PCBs resulting from breast milk as 54.3 pg TEQ/kg bw per day [83].

4. Conclusion

The current review evaluated infant formulas that have an important place in the diets of babies, with respect to the thermal processing contaminants; furan, chloropropanols and acrylamide, which have become one of the foci of researchers. When the results of the studies regarding the exposure of these contaminants are evaluated, it is suggested that babies are in the risk group, who are highly exposed to these contaminants because of their low body weight compared to other individuals, besides; there are no alternative foods to infant formulas in their daily diet.
In the light of the evidence revealed by the previous studies, the current review proposes that regarding the furan, chloropropanols and acrylamide, infant formulas can be a concern for baby health. Nevertheless, the review further suggests that it is

important to decrease the level of thermal processing contaminants or specify certain upper limits and determine these regulations by law for the individual health and the health of the overall society. Furthermore, the current review emphasized that infant formulas are not alternatives to breast milk and educating mothers in this respect is critically important for the health of next generations. One last thing to emphasize is the need to raise the awareness of breastfeeding mothers in avoiding the consumption of foods that have a rich content in terms of the abovementioned contaminants.

Author details

Burhan Başaran
Travel, Tourism and Recretaion Department, Ardeşen Vocational School, Recep Tayyip Erdoğan University, Rize, Turkey

*Address all correspondence to: burhan.basaran@erdogan.edu.tr

References

[1] World Health Organization (WHO). Country Implementation of the International Code of Marketing of Breast-Milk Substitutes: Status Report. 2011. Available from: https://apps.who.int/iris/bitstream/handle/10665/85621/9789241505987_eng.pdf [Accessed: 25 May 2020]

[2] UNICEF. Improving Child Nutrition: The Achievable Imperative for Global Progress. New York: United Nations Publications; 2013. pp. 1-14

[3] Health Canada. 2013. Breastfeeeding in Canada. Available from: https://www150.statcan.gc.ca/n1/pub/82-624-x/2013001/article/11879-eng.htm [Accessed: 25 May 2020]

[4] Bai DL, Fong DY, Tarrant M. Factors associated with breastfeeding duration and exclusivity in mothers returning to paid employment postpartum. Maternal and Child Health Journal. 2015;**19**(5):990-999

[5] Lou Z, Zeng G, Huang L, Wang Y, Zhou L, Kavanagh KF. Maternal reported indicators and causes of insufficient milk supply. Journal of Human Lactation. 2014;**30**(4):466-473

[6] Braimoh J, Davies L. When 'breast' is no longer 'best': Post-partum constructions of infant-feeding in the hospital. Social Science & Medicine. 2014;**123**:82-89

[7] Abrams SA, Daniels SR. Protecting vulnerable infants by ensuring safe infant formula use. The Journal of Pediatrics. 2019;**211**:201-206

[8] Traves D. Understanding infant formula. Paediatrics and Child Health. 2019;**29**(9):384-388

[9] Lee E. Health, morality, and infant feeding: British mothers' experiences of formula milk use in the early weeks. Sociology of Health & Illness. 2007;**29**(7):1075-1090

[10] Lee E, Furedi F. Mothers' Experience of, and Attitudes to, Using Infant Formula in the Early Months. England: School of Social Policy, Sociology and Social Research, University of Kent. 2005. pp. 1-93

[11] Perez Locas C. Mechanism of formation of thermally generated potential toxicants in food related model systems [PhD thesis]. McGill University. 2008. Available from: https://escholarship.mcgill.ca/concern/theses/z890rx30j?locale=en [Accessed: 23 May 2020]

[12] Studer A, Blank I, Stadler RH. Thermal processing contaminants in foodstuffs and potential strategies of control. Czech Journal of Food Sciences. 2004;**22**(I):1

[13] Mogol BA, Gökmen V. Thermal process contaminants: Acrylamide, chloropropanols and furan. Current Opinion in Food Science. 2016;**7**:86-92

[14] National Institutes of Health (NIH). 2020. Available from: https://pubchem.ncbi.nlm.nih.gov/compound/Furan [Accessed: 20 May 2020]

[15] Becalski A, Seaman S. Furan precursors in food: A model study and development of a simple headspace method for determination of furan. Journal of AOAC International. 2005;**88**(1):102-106

[16] Perez Locas C, Yaylayan VA. Origin and mechanistic pathways of formation of the parent furan a food toxicant. Journal of Agricultural and Food Chemistry. 2004;**52**(22):6830-6836

[17] Joint, FAO, WHO Expert Committee on Food Additives World Health Organization. Safety Evaluation

of Certain Contaminants in Food: Prepared by the Seventy-Second Meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). 2011. Available from: https://apps.who.int/iris/bitstream/handle/10665/44520/9789241660631_eng.pdf [Accessed: 20 May 2020]

[18] National Toxicology Program. Toxicology and Carcinogenesis Studies of Furan (CAS No. 110-00-9) in F344 Rats and B6C3F1 Mice (Gavage Studies). Vol. 402. National Toxicology Program Technical Report Series; 1993. p. 1

[19] International Agency for Research on Cancer (IARC). Monographs on the Evaluation of Carcinogenic Risks to Humans. 1995. Available from: https://monographs.iarc.fr/list-of-classifications [Accessed: 20 May 2020]

[20] The US Food and Drug Administration (FDA). Exploratory Data on Furan in Food. 2004. Available from: https://www.fda.gov/food/chemicals/exploratory-data-furan-food [Accessed: 20 May 2020]

[21] The European Commission Recommendation. 2007/196/EC, on the Monitoring of the Presence of Furan in Foodstuffs. 2007. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32007H0196 [Accessed: 20 May 2020]

[22] Food and Agriculture Organization of the United Nations/World Health Organization (FAO/WHO). Joint FAO/WHO Expert Committee on Food Additives (JECFA) Rome Feb 2010: Furan. Technical Report Series 959/Food Additives Series 63. 2011. Available from: http://www.fao.org/3/a-at868e.pdf [Accessed: 20 May 2020]

[23] Crews C, Castle L. A review of the occurrence, formation and analysis of furan in heat-processed foods. Trends in Food Science & Technology. 2007;**18**(7):365-372

[24] Liu YT, Tsai SW. Assessment of dietary furan exposures from heat processed foods in Taiwan. Chemosphere. 2010;**79**(1):54-59

[25] European Food Safety Authority. Update on furan levels in food from monitoring years 2004-2010 and exposure assessment. EFSA Journal. 2011;**9**(9):2347

[26] Lambert M, Inthavong C, Desbourdes C, Hommet F, Sirot V, Leblanc JC, et al. Levels of furan in foods from the first French Total diet study on infants and toddlers. Food Chemistry. 2018;**266**:381-388

[27] EFSA Panel on Contaminants in the Food Chain (CONTAM), Knutsen HK, Alexander J, Barregård L, Bignami M, Brüschweiler B, et al. Risks for public health related to the presence of furan and methylfurans in food. EFSA Journal. 2017;**15**(10):e05005

[28] Health Canada. Furan. 2016. Available from: https://www.canada.ca/en/health-canada/services/food-nutrition/food-safety/chemical-contaminants/food-processing-induced-chemicals/furan.html [Accessed: 18 May 2020]

[29] Agence nationale de securit e sanitaire alimentation, environnement, travail (Anses). 2016. Etude de l'alimentation totale infantile. Available from: http://www.quasaprove.org/moodle/pluginfile.php/1421/mod_resource/content/1/EATi_Synth%C3%A8se%20et%20Conclusions.pdf [Accessed: 18 May 2020]

[30] Sirot V, Rivière G, Leconte S, Vin K, Traore T, Jean J, et al. French infant total diet study: Dietary exposure to heat-induced compounds (acrylamide, furan and polycyclic aromatic hydrocarbons) and associated health risks. Food and Chemical Toxicology. 2019;**130**:308-316

[31] Yau JCW, Kwong KP, Chung SWC, Ho YY, Xiao Y. Dietary exposure to

chloropropanols of secondary school students in Hong Kong. Food Additives and Contaminants: Part B Surveillance. 2008;**1**(2):93-99

[32] Seefelder W, Scholz G, Schilter B. Structural diversity of dietary fatty esters of chloropropanols and related substances. European Journal of Lipid Science and Technology. 2011;**113**(3):319-322

[33] Destaillats F, Craft BD, Sandoz L, Nagy K. Formation mechanisms of monochloropropanediol (MCPD) fatty acid diesters in refined palm (Elaeis guineensis) oil and related fractions. Food Additives & Contaminants: Part A. 2012;**29**(1):29-37

[34] Rahn AKK, Yaylayan VA. What do we know about the molecular mechanism of 3-MCPD ester formation? European Journal of Lipid Science and Technology. 2011;**113**(3):323-329

[35] Pudel F, Benecke P, Fehling P, Freudenstein A, Mattheaus B, Schwaf A. On the necessity of edible oil refining and possible sources of 3-MCPD and glycidyl esters. European Journal of Lipid Science and Technology. 2011;**113**(3):368e373

[36] The Joint Food and Agriculture Organization/World Health Organization Expert Committee on Food Additives. 3-Chloro-1,2-Propanediol. Safety Evaluation of Certain Food Additives and Contaminants. WHO Food Additives Series 48. Geneva: WHO; 2001

[37] The Joint Food and Agriculture Organization/World Health Organization Expert Committee on Food Additives. Sixty-Seventh Meeting – Summary and Conclusions. Rome: FAO; 2006. Available from: ftp://ftp.fao.org/ag/agn/jecfa/jecfa67_final.pdf [Accessed: 18 May 2020]

[38] Lee BQ, Khor SM. 3-Chloropropane-1, 2-diol (3-MCPD) in soy sauce: A review on the formation, reduction, and detection of this potential carcinogen. Comprehensive Reviews in Food Science and Food Safety. 2015;**14**(1):48-66

[39] Onami S, Cho YM, Toyoda T, Horibata K, Ishii Y, Umemura T, et al. Absence of in vivo genotoxicity of 3-monochloropropane-1, 2-diol and associated fatty acid esters in a 4-week comprehensive toxicity study using F344 gpt delta rats. Mutagenesis. 2014;**29**(4):295-302

[40] International Agency for Research on Cancer (IARC). Monographs on the Evaluation of Carcinogenic Risks to Humans. 2013. Available from: https://monographs.iarc.fr/list-of-classifications [Accessed: 21 May 2020]

[41] International Agency for Research on Cancer (IARC). 2013. Available from: https://monographs.iarc.fr/list-of-classifications [Accessed: 21 May 2020]

[42] International Agency for Research on Cancer (IARC). 2000. Available from: https://monographs.iarc.fr/list-of-classifications [Accessed: 21 May 2020]

[43] Andres S, Appel KE, Lampen A. Toxicology, occurrence and risk characterisation of the chloropropanols in food: 2-monochloro-1, 3-propanediol, 1, 3-dichloro-2-propanol and 2, 3-dichloro-1-propanol. Food and Chemical Toxicology. 2013;**58**:467-478

[44] European Food Safety Authority Panel on Contaminants in the Food Chain. Scientific opinion on the update of the risk assessment on 3-monochloropropane diol and its fatty acid esters. EFSA Journal. 2018;**16**(1):5083. Available from: https://efsa.onlinelibrary.wiley.com/doi/pdf/10.2903/j.efsa.2018.5083 [Accessed: 25 May 2020]

[45] Food Additives. Evaluation of Certain Contaminants in Food

(Eighty-Third Report of the Joint FAO/WHO Expert Committee on Food Additives). WHO Technical Report Series, No.1002; 2017

[46] FAO/WHO. Joint FAO/WHO Food Standards Programme-Codex Committee on Contaminants in Food. Discussion Paper on Chloropropanols Derived from the Manufacture of Acid-HVP and the Heat Processing of Foods. CX/CF 07/1/13. Rome: Codex Alimentarius Commission; 2007. Available from: http://www.fao.org/tempref/codex/Meetings/CCCF/cccf1/cf01_13e.pdf [Accessed: 25 May 2020]

[47] Food Standards Australia New Zealand (FSANZ). Chloropropanols in Food, an Analysis of the Public Health Risk, Technical Report Series No. 15. 2003. Available from: http://www.foodstandards.gov.au/_srcfiles/Chloropropanol%20Report%20%28no%20appendices%29-%2011%20Sep%2003b-2.pdf [Accessed: 25 May 2020]

[48] Hoogenboom LAP. Scientific opinion: Risks for human health related to the presence of 3-and 2-monochloropropanediol (MCPD), and their fatty acid esters, and glycidyl fatty acid esters in food. EFSA Journal. 2016;**14**(5):4426

[49] Wöhrlin F, Fry H, Lahrssen-Wiederholt M, Preiß-Weigert A. Occurrence of fatty acid esters of 3-MCPD, 2-MCPD and glycidol in infant formula. Food Additives & Contaminants: Part A. 2015;**32**(11):1810-1822

[50] Zelinková Z, Dolezal M, Velísek J. Occurrence of 3-chloropropane-1,2-diol fatty acid esters in infant and baby foods. European Food Research and Technology. 2009;**228**:571-578

[51] Weißhaar R. Fatty acid esters of 3-MCPD: Overview of occurrence and exposure estimates. European Journal of Lipid Science and Technology. 2011;**113**:304-308

[52] Spungen JH, MacMahon S, Leigh J, Flannery B, Kim G, Chirtel S, et al. Estimated US infant exposures to 3-MCPD esters and glycidyl esters from consumption of infant formula. Food Additives & Contaminants: Part A. 2018;**35**(6):1085-1092

[53] Arisseto AP, Silva WC, Scaranelo GR, Vicente E. 3-MCPD and glycidyl esters in infant formulas from the Brazilian market: Occurrence and risk assessment. Food Control. 2017;**77**:76-81

[54] National Institutes of Health (NIH). 2018. Available from: https://pubchem.ncbi.nlm.nih.gov/compound/acrylamide#section=Top [Accessed: 19 May 2020]

[55] Tareke E, Rydberg P, Karlsson P, Eriksson S, Tornqvist M. Analysis of acrylamide, a carcinogen formed in heated foodstuffs. Journal of Agricultural and Food Chemistry. 2002;**51**(17):4998-5006

[56] Stadler RH, Blank I, Varga N, Robert F, Hau J, Guy PA, et al. Food chemistry: Acrylamide from Maillard reaction products. Nature. 2002;**419**(6906):449-450

[57] Guenther H, Anklam E, Wenzl T, Stadler RH. Acrylamide in coffee: Review of progress in analysis. Formation and level reduction. Food Additives and Contaminants. 2007;**24**(1):60-70

[58] National Toxicology Program (NTP). NTP Technical Report on the Toxicology and Carcinogenesis. Studies of Glycidamide (CAS No. 5694-00-8) in F344/N Nctr Rats and B6C3F1/Nctr Mice (Drinking Water Studies). NTP TR 588. National Institutes of Health. Public Health Service. U.S. Department of Health and Human Services; 2014.

Available from: http://ntp.niehs.nih.gov/ntp/htdocs/lt_rpts/tr588_508.pdf [Accessed: 19 May 2020]

[59] Von Tungeln LS, Doerge DR, da Costa GG, Matilde Marques M, Witt WM, Koturbash I, et al. Tumorigenicity of acrylamide and its metabolite glycidamide in the neonatal mouse bioassay. International Journal of Cancer. 2012;**131**:2008-2015

[60] Kadawathagedara M, Botton J, de Lauzon-Guillain B, Meltzer HM, Alexander J, Brantsaeter AL, et al. Dietary acrylamide intake during pregnancy and postnatal growth and obesity: Results from the Norwegian mother and child cohort study (MoBa). Environment International. 2018;**113**:325-334

[61] Goffeng LO, Alvestrand M, Ulvestad B, Sorensen KA, Skaug V, Kjuus H. Self-reported symptoms and neuropsychological function among tunnel workers previously exposed to acrylamide and N-methylolacrylamide. Scandinavian Journal of Work, Environment and Health. 2011;**37**:136-146

[62] Wilson KM, Mucci LA, Rosner BA, Willett WC. A prospective study of dietary acrylamide intake and the risk of breast, endometrial, and ovarian cancers. Cancer Epidemiology, Biomarkers & Prevention. 2010;**19**(10):2503-2515

[63] Hirvonen T, Kontto J, Jestoi M, Valsta L, Peltonen K, Pietinen P, et al. Dietary acrylamide intake and the risk of cancer among Finnish male smokers. Cancer Causes & Control. 2010;**21**(12):2223-2229

[64] Liu ZM, Tse LA, Ho SC, Wu S, Chen B, Chan D, et al. Dietary acrylamide exposure was associated with increased cancer mortality in Chinese elderly men and women: A 11-year prospective study of Mr. and Ms. OS Hong Kong. Journal of Cancer Research and Clinical Oncology. 2017;**143**(11):2317-2326

[65] Mucci LA, Sandin S, Bälter K, Adami HO, Magnusson C, Weiderpass E. Acrylamide intake and breast cancer risk in Swedish women. JAMA. 2005;**293**(11):1322-1327

[66] Schouten LJ, Hogervorst JG, Konings EJ, Goldbohm RA, van den Brandt PA. Dietary acrylamide intake and the risk of head-neck and thyroid cancers: Results from the Netherlands cohort study. American Journal of Epidemiology. 2009;**170**(7):873-884

[67] Kotemori A, Ishihara J, Zha L, Liu R, Sawada N, Iwasaki M, et al. Dietary acrylamide intake and the risk of endometrial or ovarian cancers in Japanese women. Cancer Science. 2018;**109**(10):3316-3325

[68] International Agency for Research on Cancer (IARC). 1994. Available from: https://monographs.iarc.fr/list-of-classifications [Accessed: 21 May 2020]

[69] EFSA Panel on Contaminants in the Food Chain (CONTAM). Scientific opinion on acrylamide in food. EFSA Journal. 2015;**13**(6):4104

[70] Fohgelberg P, Rosén J, Hellenäs KE, Abramsson-Zetterberg L. The acrylamide intake via some common baby food for children in Sweden during their first year of life—An improved method for analysis of acrylamide. Food and Chemical Toxicology. 2005;**43**(6):951-959

[71] Elias A, Roasto M, Reinik M, Nelis K, Nurk E, Elias T. Acrylamide in commercial foods and intake by infants in Estonia. Food Additives & Contaminants: Part A. 2017;**34**(11):1875-1884

[72] Mojska H, Gielecińska I, Stoś K. Determination of acrylamide level

in commercial baby foods and an assessment of infant dietary exposure. Food and Chemical Toxicology. 2012;**50**(8):2722-2728

[73] Health Canada. Health Canada's Revised Exposure Assessment of Acrylamide in Food. Bureau of Chemical Safety. Food Directorate. Health Products and Food Branch; 2012. pp. 1-19. Available from: https://www.canada.ca/content/dam/hc-sc/migration/hc-sc/fn-an/alt_formats/pdf/securit/chem-chim/food-aliment/acrylamide/rev-eval-exposure-exposition-eng.pdf [Accessed: 15 May 2020]

[74] Shen H, Guan R, Ding G, Chen Q, Lou X, Chen Z, et al. Polychlorinated dibenzo-p-dioxins/furans (PCDD/Fs) and polychlorinated biphenyls (PCBs) in Zhejiang foods (2006-2015): Market basket and polluted areas. Science of the Total Environment. 2017;**574**:120-127

[75] Schuhmacher M, Mari M, Nadal M, Domingo JL. Concentrations of dioxins and furans in breast milk of women living near a hazardous waste incinerator in Catalonia, Spain. Environment International. 2019;**125**:334-341

[76] Sörgel F, Weissenbacher R, Kinzig-Schippers M, Hofmann A, Illauer M, Skott A, et al. Acrylamide: Increased concentrations in homemade food and first evidence of its variable absorption from food, variable metabolism and placental and breast milk transfer in humans. Chemotherapy. 2002;**48**(6):267-274

[77] Zelinková Z, Novotný O, Schůrek J, Velíšek J, Hajšlová J, Doležal M. Occurrence of 3-MCPD fatty acid esters in human breast milk. Food Additives & Contaminants: Part A. 2008;**25**:669-676

[78] Jędrkiewicz R, Głowacz-Różyńska A, Gromadzka J, Kloskowski A, Namieśnik J. Indirect determination of MCPD fatty acid esters in lipid fractions of commercially available infant formulas for the assessment of infants' health risk. Food Analytical Methods. 2016;**9**(12):3460-3469

[79] van den Berg M, Kypke K, Kotz A, Tritscher A, Lee SY, Magulova K, et al. WHO/UNEP global surveys of PCDDs, PCDFs, PCBs and DDTs in human milk and benefit–risk evaluation of breastfeeding. Archives of Toxicology. 2017;**91**(1):83-96

[80] Costopoulou D, Vassiliadou I, Papadopoulos A, Makropoulos V, Leondiadis L. Levels of dioxins, furans and PCBs in human serum and milk of people living in Greece. Chemosphere. 2006;**65**(9):1462-1469

[81] van Leeuwen FR, Feeley M, Schrenk D, Larsen JC, Farland W, Younes M. Dioxins: WHO's tolerable daily intake (TDI) revisited. Chemosphere. 2000;**40**(9-11):1095-1101

[82] Focant JF, Fréry N, Bidondo ML, Eppe G, Scholl G, Saoudi A, et al. Levels of polychlorinated dibenzo-p-dioxins, polychlorinated dibenzofurans and polychlorinated biphenyls in human milk from different regions of France. Science of the Total Environment. 2013;**452**:155-162

[83] Huang R, Wang P, Zhang J, Chen S, Zhu P, Huo W, et al. The human body burden of polychlorinated dibenzo-p-dioxins/furans (PCDD/Fs) and dioxin-like polychlorinated biphenyls (DL-PCBs) in residents' human milk from Guangdong Province, China. Toxicology Research. 2019;**8**(4):552-559