Toxicity of acrylamide and evaluation of its exposure in baby foods

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Contaminants are a vast subject area of food safety and quality and can be present in our food chain from raw materials to finished products. Acrylamide, an α,β-unsaturated (conjugated) reactive molecule, can be detected as a contaminant in several foodstuffs including baby foods and infant formulas. It is anticipated that children will generally have intakes that are two to three times those of adults when expressed on a body-weight basis. Though exposure to acrylamide is inevitable, it is necessary to protect infant and children from high exposure. The present review focuses on the several adverse health effects of acrylamide including mutagenicity, genotoxicity, carcinogenicity, neurotoxicity and reproductive toxicity, and the possible outcomes of childhood exposure from baby foods and infant formulas.

Acrylamide: Baby food: Infant formulas: Toxicity

Introduction

Safe and adequate nutrition is crucial for the proper development of children. Other than breast milk, infant formulas and baby foods are the most important part of a baby's diet in the first year of life. Infant formulas, available in powder, liquid-concentrate and ready-to-feed forms, are artificial substitutes mimicking human breast milk. They are based on cows' milk or soya milk, designed for the consumption of infants. The medical community considers infant formulas as nutritionally acceptable for infants under the age of 1 year when breast-feeding is not possible. Infant formulas can be modified based on scientific evidence about the nutrient needs of infants[1,2]. Baby food is any food given to infants, with a soft, liquid texture, or that is chewed, from the age of 6 months to 2 years[2–4]. Baby foods are also consumed for 3 years as a part of the child's diet[1,2]. Baby foods include several baby purées made from fruits, vegetables or vegetables plus meat (beef, chicken or fish) sold commercially.

Formulation, handling and storage of baby foods are important for the foods' nutritional quality and physico-chemical properties[3]. There are several nutrients that an infant formula must contain according to the Food and Drug Administration through the advice of the American Academy of Pediatrics; it is also necessary to set upper limits for a nutrient in the formula[5,6]. On the other hand, infant formulas or baby foods can contain several contaminants that carry potential risk during the first years of life. A contaminant is an impurity; any material of an extraneous nature associated with a chemical, a pharmaceutical preparation, a physiological principle, or an infectious agent. Several contaminants, which can come from different stages of production and storage, may be present in infant formulas and baby foods. Food consumption is an important route of human exposure to contaminants such as acrylamide, pesticides and industrial pollutants[7,8]. As acrylamide is an anticipated contaminant of baby foods and infant formulas, and as children generally have acrylamide intakes that are two to three times those of adults when expressed on a body-weight (BW) basis, we will focus on acrylamide and its presence in baby foods and infant formulas in the present review[9].

Properties of acrylamide

Acrylamide (acrylic amide; International Union of Pure and Applied Chemistry (IUPAC) name 2-propenamide), an α,β-unsaturated (conjugated) reactive molecule, has the chemical formula C_3H_5NO[10,11]. It has a high mobility in soil and groundwater and is biodegradable[12]. It is also used in industry to manufacture polyacrylamide or its co-polymers[12,13].

Acrylamide is inadvertently found in starchy foods such as crisps, chips and bread[14]. Its discovery in heated foods has received a high level of attention from the public and the medical community. Acrylamide in fried and baked foods is produced by the reaction between asparagines and reducing sugars (fructose, glucose) or reactive carbonyls[15,16]. Coffee drinking and smoking are other major sources apart from the human diet[17,18]. Boiling does not produce acrylamide, but baking, frying, deep-frying, over-cooking and microwaving produce large amounts of acrylamide in

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Abbreviations: BW, body weight; GSH, glutathione; NOAEL, no observed adverse effect level.
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foodstuffs[14]. On the other hand, water is one of the major sources of exposure, as polyacrylamide is used mainly for the purification of drinking water as a flocculating agent[12,13].

Acrylamide is classified as 'probably carcinogenic to humans (group 2A)' by the International Agency for Research on Cancer. There is inadequate evidence in humans for the carcinogenicity of acrylamide[10].

Biotransformation of acrylamide

Absorption

According to data derived from animal studies, acrylamide is quickly absorbed by the skin and by the mucosa if inhaled. If taken by the oral route, it can diffuse evenly in the body because of its hydrosolubility[11].

Distribution

Tissue distribution is not significantly affected by dose or route of administration. The highest concentrations are found in erythrocytes. Despite the prominence of neurological effects, acrylamide is not concentrated in nervous system tissues[19]. Acrylamide readily crosses the placenta[20].

Metabolism

In blood, acrylamide has a half-life of approximately 2 h. In tissues, total acrylamide (parent compound and metabolites) exhibits biphasic elimination with an initial half-life of approximately 5 h and a terminal half-life of 8 d. Acrylamide does not accumulate in the body[14,20,21].

At low doses 50 % of acrylamide is oxidised to a DNA-reactive epoxide, glycidamide, by cytochrome 2E1 (CYP2E1). CYP2E1 polymorphisms in mice can cause different amounts of glycidamide to be formed. Wild-type mice have been found to metabolise 50 % of the administered dose of acrylamide to glycidamide; however, CYP2E1-null mice could not metabolise acrylamide to glycidamide[22]. Glycidamide can be metabolised by epoxide hydrolase or can undergo conjugation with glutathione (GSH)[12,21,23–25].

Excretion

The major pathway of metabolism for acrylamide is its conjugation with reduced GSH by glutathione S-transferase. Conditions such as malnutrition, oxidative stress and liver disease (alcoholic hepatitis, cirrhosis, and other malignant liver disorders) can decrease the GSH content of liver. Since a child's liver cannot carry as high a burden as an adult liver, especially under such conditions, a higher toxicity of acrylamide might be anticipated in children. Elimination occurs mainly in the urine as mercapturic acid conjugates. Greater than 90 % of absorbed acrylamide is excreted in the urine as metabolites. Less than 2 % is excreted as unchanged acrylamide. Smaller amounts are excreted in the bile and faeces. Approximately 60 % of an administered dose appears in the urine within 24 h[14]. Biotransformation of acrylamide is summarised in Fig. 1.

Toxicity of acrylamide

There are several health risks caused by the intake of acrylamide from several routes. Smoking by the mother is a major way by which the neonate is exposed to
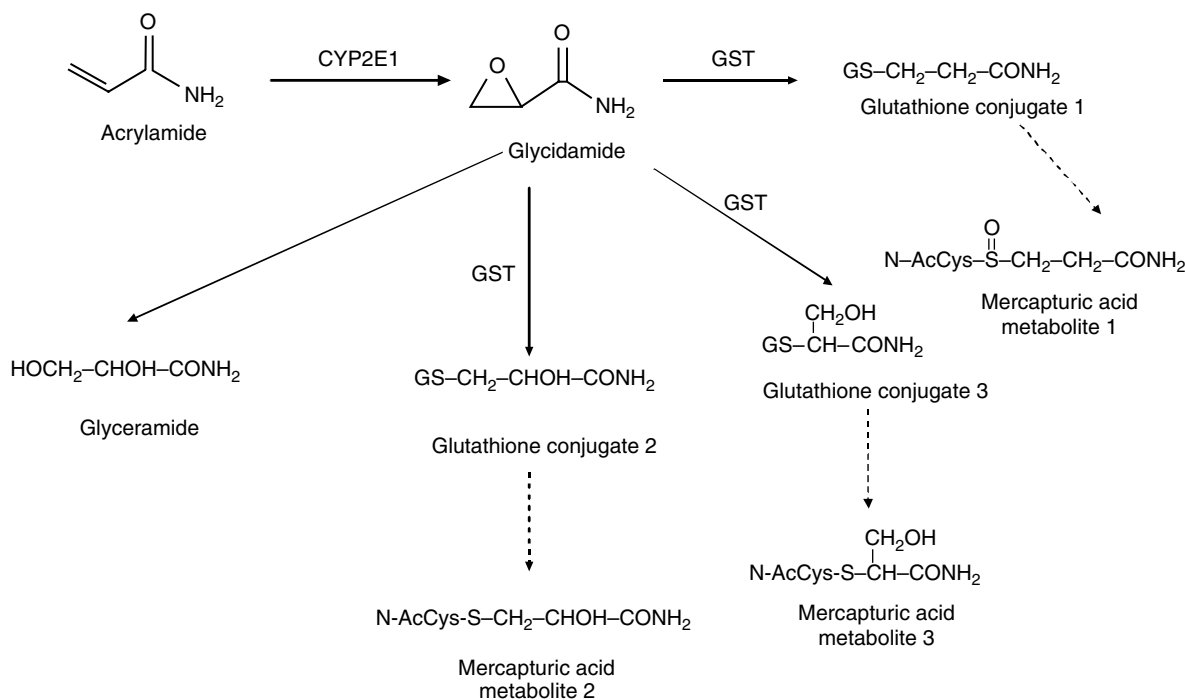

Fig. 1. Biotransformation mechanism of acrylamide. CYP2E1, cytochrome 2E1; GST, glutathione S-transferase.

acrylamide[26]. In addition, contaminated foodstuffs and drinking water are two other main ways to expose the baby or child to acrylamide. As children, especially those under the age of 2 years, are the most sensitive population, acrylamide intake levels must be monitored particularly in infant formulas and baby foods. On the other hand, mothers should be attentive while choosing the water with which they prepare food for their child. The health risks of acrylamide can be classified as follows.

Mutagenic, genotoxic and carcinogenic properties of acrylamide

The genotoxic, mutagenic and carcinogenic potentials of acrylamide have been studied extensively. Acrylamide itself reacts rapidly with thiol (−SH) and amino groups; this explains why its primary targets are proteins[25]. Acrylamide has been shown to bind DNA by a Michael-type process *in vitro* with low activity[21,25]. Nevertheless, there is sufficient evidence in the literature that both acrylamide and its metabolite glycidamide are mutagenic and clastogenic in mammalian cells[19,22]. Data suggest that mice are more vulnerable to acrylamide tumorigenicity. The metabolic activation of acrylamide is more efficient and the detoxification process is poorer in mice than rats, since mice have higher levels of glycidamide and lower levels of GSH−glycidamide conjugates[27].

Acrylamide causes induction of the following genotoxic effects[28,29]:

(a) gene mutations and chromosomal aberrations in germ cells of mice *in vivo*;
(b) chromosomal aberrations in germ cells of rats *in vivo*;
(c) chromosomal aberrations in somatic cells of rodents *in vivo*;
(d) gene mutations and chromosomal aberrations in cultured cells *in vitro*;
(e) cell transformation in mouse cell lines;
(f) somatic mutation in the spot test *in vivo*;
(g) heritable translocation and specific locus mutations in mice and dominant lethal mutations in both mice and rats;
(h) unscheduled DNA synthesis in rat spermatocytes *in vivo*; but not in rat hepatocytes. However, glycidamide induces unscheduled DNA synthesis in rat hepatocytes.

The studies on mutagenic, genotoxic and carcinogenic properties of acrylamide and glycidamide are summarised in Table 1[29−43].

Adduct formation with Hb

Acrylamide forms different protein adducts, the most important of which are Hb adducts extensively formed at −SH groups and on the amino groups of the N-terminal valines in erythrocytes. The measurement of Hb adducts can give an integrated measure of the exposure in the previous 3−4 months, since the lifespan of erythrocytes is about 4 months[25,44].

Adduct formation with acrylamide shows a linear dose−response relationship and glycidamide adducts generate a concave curve. This shows that the percentage of acrylamide metabolised to glycidamide is inversely proportional to the administered dose of acrylamide[45,46].

Neurotoxic effects of acrylamide

Early morphological studies suggested that neurological defects caused by acrylamide intoxication are mediated through distal axonal degeneration (also known as 'dying-back' neuropathy) in the peripheral nervous system and central peripheral nervous system[47,48]. Later studies showed that nerve terminals and Purkinje neurons are the targets of acrylamide[49]. Nowadays, there are two important hypotheses regarding acrylamide neurotoxicity: (a) inhibition of kinesin-based fast axonal transport; (b) direct inhibition of neurotransmission[50,51].

Acrylamide, the parent compound, is a soft electrophilic neurotoxicant, reacting on thiol groups of proteins (cysteine, homocysteine) and GSH as well as protein-bound −SH groups (kinesin, dynein), whereas the metabolite glycidamide is a harder electrophilic compound, reacting with nucleophilic centres of adenine and guanine in the DNA[37−41]. It has been shown that acrylamide inhibits the action of brain glutathione *S*-transferase and reduces the levels of brain GSH[52]. It has also been suggested that acrylamide neurotoxicity is caused by its effects on heavy- and medium-weight neurofilaments, the change it causes on neurotransmitter receptor expression and through inhibition of neurotransmission[43−45]. Electrophilic neurotoxins, including acrylamide, may cause protein structure and function changes by oxidation and this may lead to pathway failure and finally nerve cell damage. Therefore such chemicals at low doses and long-term exposure might be a cause of neurodegenerative diseases such as Alzheimer's disease[12,35,53,54]. The studies on neurotoxic effects of acrylamide and glycidamide are summarised in Table 1[29,35,55−57].

Reproductive and developmental toxicity of acrylamide

Reproductive toxicity has also been observed in laboratory animals exposed to high levels of acrylamide[55]. Several studies have been conducted on reproductive toxicity; these are presented in Table 1[58−62].

There seems to be a relationship between the neurotoxicity and reproductive toxicity of acrylamide[56,62−65]. One theory is that reproductive toxicity is related to neurotoxicity, as neurotoxicity influences mating behaviour. Several studies have clarified that some of the neurotoxic effects of acrylamide in rats are a weakness of the hind-limbs, reduced hind-limb grip strength, and increased foot splay[62,63,65]. This reduced hind-limb function could cause impairment in mounting responses, copulatory behaviour, and intromission (entry)[58]. Dysfunctional intromission could also have an impact on the proper deposition of sperm in the vagina and uterus and subsequent hormonal events that cause the stimulation of reproductive hormones and implantation. In addition, erectile function could be decreased due to nerve damage in the penis[66]. Another theory is that both types of toxicity are mediated through effects on the kinesin motor proteins[62]. These kinesin proteins are found in the flagella of sperm as well as the nervous system and other tissues[65].

Table 1. Summary of literature on mutagenicity, genotoxicity, carcinogenicity, neurotoxicity, reproductive and developmental toxicity of acrylamide

Study	Study design	Results
Mutagenic, genotoxic and carcinogenic properties of acrylamide		
Hashimoto & Tanii (1985)[29]	Mutagenicity testing of acrylamide and glycidamide on *Salmonella* strains	Acrylamide was not mutagenic in Ames' test, in the presence of the S9 fraction; however, glycidamide was shown to be mutagenic in some of the strains of *Salmonella*, with or without the S9 mix
National Toxicology Program (1989)[30]	Acrylamide was administered to F344/N rats and B6C3F1 mice by oral administration	Acrylamide showed organ-specific and species-specific tumorigenicity in rodents. Application of acrylamide through different routes (topically, orally, systemically) increased the risk of carcinomas and lung and skin adenomas in mice and induced thyroid adenomas/adenocarcinomas, uterine adenocarcinomas, clitoral adenomas, oral papillomas and mammary gland tumours in rats
Russell *et al.* (1991)[31]	Induction of specific-locus mutations in male germ cells of the mouse	Significantly increased the specific-locus mutation rate in certain post-stem-cell stages of spermatogenesis, but not in spermatogonial stem cells
Hoorn *et al.* (1993)[32]	A transgenic mouse strain with a high copy number of rescuable *lacZ* sequences was evaluated for its effectiveness in detecting *lacZ* mutations	Acrylamide was found to increase the frequency of *lacZ* mutations in bone marrow about 1·8-fold over background
Dearfield *et al.* (1995)[33]	*Hypoxanthine-guanine phosphoribosyl transferase* locus in cultured CHO cells	Acrylamide has shown to be mutagenic at the *hypoxanthine-guanine phosphoribosyl transferase* locus in cultured CHO cells with or without exogenous activation system
Segerbäck *et al.* (1995)[34]	Testing DNA damage potential of acrylamide and glycidamide on rats and mice	Glycidamide was found to induce *N*-7-(2-carbamoyl-2-hydroxy-ethyl)gua-nine
Fu *et al.* (2000)[35]	Neonatal mouse tumorigenicity bioassay	Glycidamide showed 5- to 7-fold higher DNA adduct levels than when treated with acrylamide, indicating lower levels of CYP450 enzymes in immature tissues
Gamboa de Costa *et al.* (2003)[36]	Induction of DNA adduct formation of acrylamide and glycidamide in adult and neonatal mice	Both acrylamide and glycidamide caused DNA adduct formation; however, adduct levels formed by glycidamide were modestly higher
Ma *et al.* (2008)[37]	Comet assay on lung, liver, spleen, kidney, testicle, bone marrow and peripheral lymphocytes of mice	Acrylamide caused DNA damage to multiple organs of mice
Cao *et al.* (2008)[38]	Comet assay on HepG2 cells	Acrylamide caused DNA damage
Zhang *et al.* (2008)[39]	Micronucleus assay on HepG2 cells	Acrylamide increased micronucleus frequencies
Baum *et al.* (2008)[40]	Comet assay on V79 cells and in human lymphocytes	Glycidamide caused DNA damage
Wolf *et al.* (2008)[41]	Micronucleus assay on hens' eggs	Acrylamide increased micronucleus frequencies
Recio *et al.* (2010)[42]	Micronucleus/comet assays on rats and mice	Acrylamide was found to induce micronucleated reticulocytes in rats
Mei *et al.* (2010)[43]	Micronucleus and *Hprt* assays on rats	Neither acrylamide nor glycidamide increased the frequency of micro-nucleated reticulocytes. In contrast, both compounds produced small (approximately 2- to 3-fold above background) but significant increases in lymphocyte Hprt mutant frequency
Neurotoxic effects of acrylamide		
Burek *et al.* (1980)[55]	Male and female Fischer 344 rats were administered acrylamide in their drinking water at 0, 0·05, 0·2, 1, 5, or 20 mg/kg per d for up to 93 d. Following the administration of acrylamide in the drinking water, male rats from each dose level were held for up to 144 d of recovery	Nerve degeneration was observed; however, after 144 d, the lesions were partially or fully recovered

Chapin *et al.* (1995)[56]	Male and female Swiss CD-1 mice received acrylamide in drinking water (3, 10, 30 ppm) for 14 weeks Neurotoxicity was assessed at several times in both F0 and F1 generations by measuring forelimb and hindlimb grip strength	Presence of only minor effects on grip strength and without detectable neural histopathology. Female reproduction was not significantly affected by these compounds at the doses used. Thus, these data confirm the male as the affected sex and that reproductive toxicity was greater than motor neuron toxicity when measured as grip strength In the F0 generation, acrylamide caused an 11 % decrease in pup number without measurable neurotoxicity; female fertility was not affected. Although both generations consumed the same amount of acrylamide, there were larger changes in the fertility-related endpoints in the F1 mice than in the F0 mice, with no concomitant change in organ weights or sperm parameters
Ghanayem *et al.* (2010)[57]	5- to 30-week-old intact male C57Bl/6J mice fed with low- and high-energy diets	Acrylamide potentiated the reproductive toxicity induced by obesity in obese rats
Reproductive toxicity of acrylamide Zenick *et al.* (1986)[58]	Male rats received acrylamide in drinking water (50, 100, or 200 ppm) for up to 10 weeks. Copulatory behaviour, semen, and (for controls and 100 ppm only) fertility and fetal outcomes were evaluated. Females received acrylamide (25, 50, 100 ppm) for 2 weeks before initiation of breeding and then throughout gestation and lactation	Disruptions in mating performance, a decrease in pregnancy rate, an increase in post-implantation loss, and hindlimb splaying appeared in the females; a decrease in pup body weight at birth, decreases in weight gain during lactation, and a delay in vaginal patency were also observed
Sublet *et al.* (1989)[59]	Males were orally administered with 0, 5, 15, 30, 45, or 60 mg/kg acrylamide for 5 d and then mated serially to naive females	Acrylamide treatment reduced fertility and increased pre- and post-implantation loss, primarily over the first 3 weeks post-treatment. However, the effects were transient
Wise *et al.* (1995)[60]	Acrylamide at 0, 5, 10, 15, or 20 mg/kg per d were administered at 5 ml/kg by oral administration from GD 6 to lactational day 10 to groups of twelve mated females each	Significantly increased pup mortality and characteristic hindlimb splaying; significant decreases in average horizontal motor activity and auditory startle response were observed only in weanlings of the 15 mg/kg per d group
Field *et al.* (1990)[61]	Sprague–Dawley rats received acrylamide at 0, 2·5, 7·5, and 15 mg/kg body weight per d on GD 6–20. Swiss CD-1 mice received acrylamide at 0, 3, 15, and 45 mg/kg body weight per d on GD 6–17	Maternal and fetal weight decreases and extra rips were observed in a dose-dependent manner
Tyl *et al.* (2000)[62]	160 Male, 160 female virgin rats; 0, 5, 15, 30, 45, or 60 mg/kg per d for 5 d	At 15 to 60 mg/kg per d, males exhibited significantly reduced weight gain and reduced mating. Females showed a decrease in pregnancy rate. Also, increased post-implantation losses were observed at the 60 mg/kg per d dose

CHO, Chinese hamster ovary; CYP450, cytochrome 450; ppm, parts per million; GD, gestation day.

Interference with these proteins could reduce sperm motility and fertilisation events[62,66,67–70].

Other mechanisms of acrylamide on reproduction in rodents could be from the alkylation of sulfhydryl groups on unique proteins, such as protamine, in the sperm head and tail[22,71,72]. This could affect sperm penetration and induce the pre-implantation losses seen in some dominant lethal studies[62,73].

No human data are present regarding the reproductive and developmental toxicity of acrylamide. However, data are sufficient to conclude that acrylamide is a reproductive and developmental toxicant in rodents.

Dose–response and dose–effect relationships of acrylamide

Numerous investigators have looked at dose–response and dose–effect relationships in a variety of animal models. There do not appear to be significant differences between the mammalian species studied. The lethal dose, 50 % (LD_{50}) levels of acrylamide through various routes in different rodents are given in Table 2[74].

The WHO states that acrylamide belongs to the group of chemicals thought to have no reliably identifiable 'threshold' of effects, meaning that very low concentrations will also result in very low risks, but not in zero risk: some risk is always present when the chemical is ingested. However, for carcinogens such as acrylamide, risk is thought to increase with increasing exposure[75].

In June 2002, the FAO of the UN and the WHO issued a report about the health implications of acrylamide in food. The Consultation concluded that the no observed adverse effect level (NOAEL) for acrylamide neuropathy is 0·5 mg/kg BW per d and the NOAEL for fertility changes is four times higher than for peripheral neuropathy and 2000-fold greater than estimated dietary exposures[24,76,77]. The NOAEL for reproductive toxicity was estimated to be 2–5 mg/kg BW per d depending on the endpoint of fertility or embryonic death[77]. No reproductive toxicities have been reported in humans. Therefore, it is highly unlikely that any reproductive toxicity in humans would result from dietary exposure to acrylamide, although concerns about the cumulative effects of low-level chronic exposure are increasing.

Evidence of neurological effects has been observed following single oral doses of 126 mg/kg in rats and rabbits and 100 mg/kg in dogs[78,79]. Using chronic dosing schedules, it has been observed that cumulative oral doses of 500–600 mg/kg using daily doses of 25–50 mg/kg per d are required to produce ataxia in rats, dogs and

baboons[78,80,81]. Smaller daily doses do not produce a clinical effect until a larger cumulative dose is attained. It has been found that the administration of acrylamide at daily doses of 6 to 9 mg/kg does not produce evidence of neurotoxicity in rats until a cumulative dose of 1200 to 1800 mg/kg is attained, and that doses of up to 3 mg/kg per d for 90 d administered to rats do not result in adverse effects[78,82]. Spencer et al.[83] reported that Rhesus monkeys fed up to 2 mg/kg per d did not show any adverse clinical effects at 325 d.

Acrylamide appears to be a multi-organ carcinogen in rodents. This is consistent with its distribution throughout the whole body. However, it is noteworthy that there are no corresponding target organs in mice and rats. Rat thyroid follicular cell tumours and mammary tumours from two studies are considered of possible relevance for human health. Modelling of these data has allowed the determination of benchmark doses and benchmark dose lower confidence limits[84,85]. For a 10 % CI, the results were in the range of 300–1100 μg/kg per d for the mammary tumours and between 630 and 930 for the thyroid tumours using the Environmental Protection Agency's dose–response modelling for determination of a point of departure for a risk of 10 % lower exposure dose (LED_{10})[86,87]. Relating the combined tumour data to Hb adduct data of acrylamide and glycidamide the doses 440 or 950 μg/kg per d were determined, respectively, which are close to the benchmark dose lower confidence limits[86–88].

The estimated average chronic human dietary intake was calculated crudely as 0·3–0·7 μg/kg BW per d in 2002. However, the Food and Drug Administration calculated the exact intake as 0·4 μg/kg BW per d in 2003 and this value remained the same when the Food and Drug Administration updated this subject in 2004[89]. This increase of acrylamide intake by age seems to reflect the increased consumption of fast food together with potato crisps or French fries.

As the NOAEL for neuropathy is given as 0·5 mg/kg BW per d, a woman weighing 132 lb (60 kg) could safely consume 30 mg acrylamide daily; a man weighing 180 lb (82 kg) could consume about 41 mg[90]. On the other hand, if the same calculation is applied to the daily intake of a child, a child weighing 20 lb (9 kg) can consume food including 4·5 mg acrylamide. Whether it is appropriate to judge the daily intake of a child with the same calculation is a matter of debate considering that the susceptibility of a child towards several chemicals is much higher than that of an adult. It is anticipated that children will generally have intakes that are two to three times those of adults when expressed on a BW basis.

Studies on acrylamide contamination in baby foods and infant formulas and estimated daily exposures of acrylamide are given in Table 3[26,91–94].

Determination of acrylamide and limits in foods

Potentially toxic acrylamide is largely derived from heat-induced reactions between the amino group of the free amino acid asparagine and carbonyl groups of glucose and fructose in cereals, potatoes, and other plant-derived foods[95]. Several methods have been described that determine acrylamide in several foodstuffs and water.

Table 2. Lethal dose, 50 % (LD_{50}) levels of acrylamide through different routes in different rodents

Species	Route	LD_{50} (mg/kg body weight)
Rat	Oral	107–251
Rat	Dermal	400
Rat	Intraperitoneal	90–120
Mouse	Oral	107–170
Guinea-pig	Oral	150–180

Table 3. The daily intake of acrylamide of children in several European countries

Study	Data	Age	Acrylamide intake (µg/kg BW per d)
Alexy et al. (DONALD Study), (2002)[91], daily intake calculated in Hilbig et al. (2004)[26]	Calculation over the total food intake (diet records) of 3387 children	<1 year 1−7 years 7−19 years	0·21 0·43 0·30
Wilhelm et al. (RUB Study), (2002)[92], daily intake calculated in Hilbig et al. (2004)[26]	Calculation over the total food intake (diet records) of 119 children	1− < 7 years	0·61
Scientific Committee of the Norwegian Food Control Authority (2002)[93]	Data on consumption of cereal based baby food and analysed acrylamide concentrations, no further details available	Boys (6 months) Girls (6 months) Boys (12 months) Girls (12 months)	0·29 0·31 0·33 0·36
European Commission, Health and Consumer Protection Directorate (French Food Safety Agency) (2003)[94]	National food consumption data and analysed acrylamide concentrations presented by SCF; no further details available	2–14 years Mean 95th percentile	 1·4 2·9

BW, body weight; SCF, Scientific Committee on Food.

The first reported data on acrylamide in foods available on the market were developed by the Swedish National Food Administration using liquid chromatography/tandem mass spectroscopy (LC/MS/MS)[96]. Since then, several analytical procedures have been developed, including LC/MS/MS and GC/MS with different sensitivity, cost, speed and applicability[90].

There are a limited number of studies concerning the daily intake of acrylamide from foodstuffs. In the year 2002, the Swedish National Food Agency showed that certain fried, baked and deep-fried foods and coffee had high concentrations of acrylamide[96]. In a Norwegian study, acrylamide exposure from foods and coffee was estimated to be 0·49 and 0·46 µg/kg BW in males and females, respectively[97]. The New Zealand National Nutrition Survey showed that with a typical Western diet, including hot chips (French fries) and potato crisps, the calculated daily intake of acrylamide is 0·3 µg/kg BW, which is below the NOAEL[98].

On the other hand, as babies and children are a more sensitive population than adults, their consumption of foods including acrylamide must be limited. The studies calculating the daily intake of acrylamide of children in several European countries are summarised in Table 4[11,90,99−103].

The European Union gives high importance to acrylamide contamination in food. After the Commission Recommendation 2007/331/EC, twenty-one member states of the European Union presented the results of acrylamide in several foodstuffs (presented under the titles of 'French fries', 'potato crisps', 'potato products for home cooking', 'bread', 'breakfast cereals', 'biscuits', 'roasted coffee', 'jarred baby foods', 'processed cereal-based baby foods' and 'other products') to the European Food Safety Authority in 2007. There were 2715 results reported for foods sampled in 2007, with a minimum of seventy-six reported for 'processed cereal-based baby foods' and a maximum of 854 reported for 'other products'. The arithmetic mean acrylamide content ranged from 44 µg/kg for 'jarred baby foods' to 628 µg/kg for 'potato crisps', with the equivalent geometric means of 31 and 366 µg/kg. The 2007 results

Table 4. Studies on acrylamide contamination in baby foods and infant formulas and estimated daily exposures of acrylamide

Study	Food type	Analysis method	Estimated daily exposure
Rosén & Hellenäs (2002)[90]	Canned baby food	LC/MS/MS	7·8 µg/kg
Jiao et al. (2005)[99]	Infant powdered milk and baby foods	LC/MS	Ranging between 3·01 and 9·06 µg/kg for infant powdered milk and between 6·80 and 124·93 µg/kg for baby foods
Şenyuva & Gökmen (2005)[100]	Baby foods	LC/MS	149 (SD 14·7) µg/kg
Fohgelberg et al. (2005)[11]	Canned baby food	LC/MS	7·8 µg/kg
Scientific and Technological Research Council of Turkey (2006)[101]	Baby biscuits	LC/MS	150−610 µg/kg
European Food Safety Authority Scientific Report (2009)[102]	Jarred baby foods	LC/MS	Ranging between 44 and 628 µg/kg
Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (Federal Office for the Protection of the Consumer and Food Safety, Germany) (2003)[103]	Baby foods (infant formulas and follow-on formulas, commercial cereal-based food, commercial menus for infants and young children, commercial vegetable or fruit preparations) Commercial cereal-basedfood Cakes for infants and young children	LC/MS	Maximum 131 µg/kg Mean 13, maximum 633 µg/kg

LC/MS/MS, liquid chromatography/tandem mass spectroscopy.

were compared with results collected by the European Commission Joint Research Centre's Institute for Reference Materials and Measurements in the years 2003 to 2006. There were 9311 results reported for foods sampled in the 4 years; however, there were only eight results reported for the food category 'jarred baby foods' and they were not included in the comparison. The arithmetic mean of acrylamide content ranged from 55 µg/kg for 'cereal-based baby foods' to 678 µg/kg for 'potato crisps', with the equivalent geometric means of 35 and 514 µg/kg. The highest 95th percentile value was reported for 'potato crisps' at 1718 µg/kg and the highest maximum for 'other products' at 7834 µg/kg[102].

Conclusion

Infants and children are susceptible towards the effects of several xenobiotics. The knowledge of all factors that affect the formation of glycidamide is important with respect to estimating risk from this known carcinogen. It is known that the metabolism and clearance of drugs are higher in children because of the larger liver:BW ratio and the higher blood flow through the liver compared with those of older adults[104]. As the major metabolite of acrylamide, glycidamide, is formed through biotransformation, it is likely that glycidamide can be formed at an higher rate than adults in children. In addition, the detoxification pathway through conjugation with GSH may be less functional due to low levels of GSH in a child's liver. Therefore, it is possible that the toxicity of acrylamide might be higher in children.

Children and adolescents should eat a balanced and assorted diet, which includes plenty of fruit and vegetables but also cereals. Also, parents should moderate their children's consumption of fried and fatty foods. Such a diet would also reduce the risk of high exposures to acrylamide, since acrylamide has not been determined in unheated or boiled foods[105]. Acrylamide presumably will also be present in low levels in a nutritionally balanced diet; however, it is in the power of parents to feed their children with more healthy foods. On the other hand, for small children who are merely fed with infant formula and baby food, it is obligatory for governments to take serious measures to monitor contaminants[89].

Taking into account all the knowledge given above, baby food and infant formulas should be routinely tested before use for the detection of acrylamide using improved techniques. Strict law enforcement should be undertaken regarding the detection of all the contaminants in infant formulas and baby foods. Furthermore, producers should be warned by regulatory authorities regarding good manufacturing practices to decrease the levels of contaminants, particularly acrylamide.

Acknowledgements

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