A REVIEW ON ACRYLAMIDE IN FOODS: SOURCES AND IMPLICATIONS TO HEALTH

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Abstract

Acrylamide is basically one of the most industrial organic compound monomers of polyacrylamide that finds its way into many products in our everyday life. It is one of the potential environmental public health problems, both as a suspected carcinogen and a neurotoxin resulting from its increased accumulation in the process of cooking food materials. It is a chemical with a very wide range of uses and it accounts for one of the major health concern because it has been detected in a widely consumed food items; fried breads (or any carbohydrate-rich food items cooked at high temperature). Accordingly, the general population is highly exposed to it. Acrylamide formation occurs primarily at elevated cooking temperatures used when frying or baking (above 120 ℃) and in low moisture conditions. These cascades of reactions involve the Maillard reaction, which leads to browning and flavor changes in cooked foods. There are also several foods in which acrylamide appears to form in high-moisture conditions at lower temperatures, such as prune juice and canned ripe black olives. These substances are usually formed when asparagines is heated in the presence of compounds that have α-hydroxycarbonyl groups, α,β,γ,δ-diunsaturated carbonyl groups or α-dicarbonyl groups. The acrolein pathway and enzymatic decarboxylation of asparagine, as well as endogenic processes, are other alternative routes to amino acid formation. It can be naturally present in uncooked, raw foods in very small amounts. It is pertinent to note that some non-dietary sources could expose us to this substance. These non-dietary sources include cigarette smoke (about 1-2 micrograms per cigarette) and cosmetics. There is also airborne release of acrylamide during many different manufacturing processes, including the manufacturing of paper, asphalt, petroleum, photographic film, construction adhesives, varnishes, and dyes. The U.S. Environmental Protection Agency (EPA) has estimated that U.S. adults average 0.4 micrograms of dietary acrylamide intake per kilogram of body weight each day. For an adult weighing 150 pounds, this amount translates into approximately 27 micrograms of dietary acrylamide per day. Levels reported in literature vary from 25 to 2000 μg/kg and potato products are considered as containing the highest level of acrylamide. The nitty-gritty of this review is to summarize various strategies, results of academic and industrial research on health damaging properties, exposure sources, formation mechanism and mitigation measures of acrylamide in foods.

Introduction

Acrylamide is a product of contamination generated in several foods during cooking as a consequence of the Maillard reaction, derived from the reaction between the free amino acid asparagine with reducing sugars or other carbonyl compounds. This chemical reaction mainly occurs when foods are subjected to high temperatures as during frying, roasting or baking and in low moisture conditions. According to the European Food Safety Agency (EFSA), processed potatoes together with coffee and cereal based food (Potato Chips (Crisps), French Fries, Crackers, Toast, Bread Crisps, Cookies, Boxed Breakfast Cereal, Corn Chips (Crisps), Bakery Products, Coffee, Cocoa, Bread) are the main sources of exposure to acrylamide in the diet

(EFSA, 2014). Due to the presence of large concentration of acrylamide precursors in the potato, when this product is subjected to high temperatures, as during frying, acrylamide generated became a health concern (Williams, 2005). Levels of this contaminant by up to 3000 or even more than 4000 μg/kg have been detected in potato chips and crisps (Amit and Prem, 2012; Becalski *et al.,* 2010; Friedman, 2003; Hilbig *et al.,* 2004; Shamla and Nisha, 2014). It is known that dietary habits have changed over the last few years, increasing the consumption of processed foods and decreasing that of natural foods (Delgado-Andrade, 2014). Such dietary changes are particularly evident in younger generations whose habits are associated with high levels of snacking and fast food consumption which contributes to high levels of acrylamide intake (Delgado-Andrade *et al.,* 2012; Gilbert and Khokhar, 2008). Among snack foods, potato chips are one of the most popular foodstuffs and large quantities are consumed worldwide, especially by young people (Ouhtit *et al*., 2014; Wyka *et al*., 2015). According to Katz *et al*. (2012) French fries and potato chips may contribute 56% of the total acrylamide intake in the Western diet of the adolescents. Due to this fact, recent researches have been focused on different aspects affecting acrylamide formation in fried potato products and possible mitigation strategies (Mesías and Morales, 2015). However the relative importance of different sugars and/or carbonyls as reactive species and the type of model system as well as the conditions employed may play a crucial role in its formation (Koutsidis *et al*., 2008; Koutsidis *et al*., 2009). It is suggested that both molecular mobility and sugar reactivity would determine the relative effect of sugars on acrylamide formation, whereas temperature may also play an important role in determining these relative reactivates (Wedzikcka *et al*., 2005).

Asparagine, through its participation in the Maillard reaction, has been identified as the major precursor of acrylamide, and heat-treated products containing relatively high amounts of asparagine have been shown to yield correspondingly high acrylamide concentrations (Wendie *et al*., 2005). The importance of the Schiff base of asparagines which corresponds to the dehydrated N-glycosyl compound has been recognized. Decarboxylation of the Schiff base is a key step and the reaction product ends in acrylamide either directly or via 3-aminopropionamide (Zyzak *et al*., 2003; Israilides and Varzakas, 2015). The acrylamide used in the production of polyacrylamide is also extremely used in the treatment of drinking and waste water, in paper production, in petroleum industry, in the production of mine, mineral, asphalt and in the treatment of land and soil (Exon, 2006; Friedman, 2003). Moreover, it is also commonly used as an additive in cosmetic industry, in electrophoresis used in molecular biology applications, in the production of photographic film, in the manufacturing of adhesive, varnish and dye and in the preparation of some alloys in dentistry (EURAR, 2002). In addition to such industrial and laboratory uses, high levels of acrylamide were detected in tobacco smoke (Pruser and Flynn, 2011).

Factors affecting acrylamide formation and degradation in foods are acrylamide precursors such as free amino acids (mainly asparagine, reducing sugars and processing conditions, that is, baking time and temperature, moisture content and matrix of product).

Acrylamide, produced during thermal processing of carbohydrate-rich foods, is classified as "probably carcinogenic to humans" by the International Agency for Research on Cancer. Some studies demonstrated that acrylamide-induced cytotoxicity was relevant to oxidative stress. The cytotoxic properties of acrylamide by affecting the cellular redox status may lead to generation of reactive oxygen species (ROS) causing cytotoxic and genotoxic effects. Some strategies have been postulated to reduce acrylamide-mediated cytotoxicity by using natural antioxidant like vitamin E. Vitamin E can protect cellular structures against damage from free radicals such as peroxy radical, hydroxyl radical, as well as super oxide. Also, it has protective effect from oxidation products such as malondialdehyde (MDA) and hydroxynonenal. Vitamin E, as an important antioxidant, plays a role in inhibition of mutagen formation as well as repair of membranes and DNA (Dong *et al.*, 2012).

Much research has focused on the human health risks of the levels of acrylamide found in foods and on the other hand of reducing those levels; for example by modifying processing conditions or by the use of asparaginase enzyme preparations (Anuradha and Varalakshmi, 2011).

What is Acrylamide?

Acrylamide (or acrylicamide) is a chemical compound with the chemical formulaC_3H_5NO and has a molecular weight of 71.08 g. Its IUPAC name is 2- propenamide. It is a white odorless crystalline solid, soluble in water, ethanol, ether, and chloroform (Kepekci-Tekkeli *et al.*, 2012) Acrylamide is incompatible with acids, bases, oxidizing agents, iron and salts. It decomposes non-thermally to form ammonia, and thermal decomposition produces carbon monoxide, carbon dioxide, and oxides of nitrogen. It is a chemical used primarily as a building block in making polyacrylamide and acrylamide copolymers. Polyacrylamide and acrylamide copolymers are used in many industrial processes, such as the production of paper, dyes, and plastics, and in the treatment of drinking water and wastewater, including sewage. They are also found in consumer products, such as caulking, food packaging, and some adhesives. Trace amounts of acrylamide generally remain in these products (David, 2003).

A Swedish study was the first to report that frying or baking at high temperatures (greater than 250°F [121ºC]) for prolonged periods of time could create acrylamide in many types of food, particularly starchy foods, such as: french fries, potato chips, crackers, certain types of fried or baked bread, some processed cereals. The amount of acrylamide varied according to the type of food and, in some cases, the brand of a particular food. French fries had one of the highest amounts of acrylamide (Kepekci-Tekkeli *et al.*, 2012). It is a difunctional monomer, containing a reactive electrophilic double bond and an amide group. It exhibits both weakly acidic and basic properties. It is prepared on an industrial scale by the hydrolysis of acrylonitrile by nitrile hydratase (Murkovic, 2004).It is a versatile organic compound that finds its way into many products in our everyday life. The single unit form of acrylamide is toxic to the nervous system, a carcinogen in laboratory animals, and a suspected carcinogen in humans (Claudio*et al*., 2016; Park *et al*., 2002).

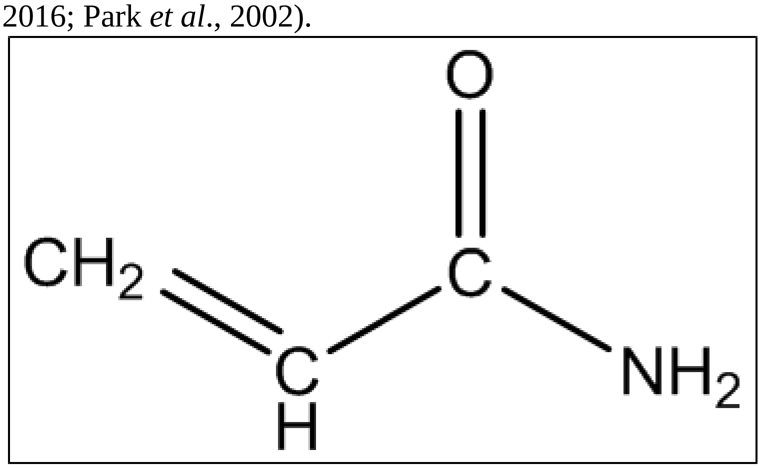

Fig. 1: Schematic representation of acylamide structure.

It readily polymerises on reaching melting point or exposure to UV light. Solid acrylamide is stable at room temperature, but may polymerise violently when melted or exposed to oxidizing agents.

Formation of Acrylamide in Foods

Elevated levels of acrylamide have been found in home cooked foods, as well as pre-cooked packaged and processed foods. Acrylamide is naturally produced in some foods that have been cooked or processed at high temperature and the levels appear to increase with the duration of heat. Also tobacco smoking generates substantial amounts of acrylamide (Pruser and Flynn, 2011). Formation of acrylamide is favoured by high temperatures and low moisture content. As temperature increases and moisture content decreases, acrylamide formation increases. In general, the darker in colour the food product (burnt toast, darker chips), the higher the acrylamide content (Emmanuel, 2010). It is primarily responsible for the flavours, aromas and brown colours in many foods, e.g. browning during toasting and in frying potatoes. In addition to these and many other beneficial compounds, numerous compounds with potential adverse health benefits also are formed (Delgado-Andrade, 2014).

In September 2002, researchers discovered that amino acid asparagines, which is present in many vegetables, with higher amounts in some varieties of potatoes, can form acrylamide when heated to high temperature in the presence of certain sugars (Michael *et al*., 2004) . The formation of acrylamide is mainly depending on free asparagine and reducing sugars, limiting factor being the sugar (Biedermann-Brem *et al*., 2003; Amrein *et al*., 2004; Becalski *et al*., 2004; De Wilde *et al*., 2005; Keramat *et al*., 2011) as asparagine is usually more abundant in potatoes than reducing sugars (Amrein *et al*., 2007). On the other hand when the molar ratio of reducing sugars to asparagine content is greater than two, meaning that there is an abundance of reducing sugars then the asparagine content might be the possible limiting factor for acrylamide formation (Matsuura-Endo *et al*., 2006). However in a different study no correlation was found between the starting materials (asparagine and sugars) content and acrylamide formation (Skog *et al*., 2008). The reducing sugars (glucose, fructose) and asparagine are natural components of plants or plant-derived ingredients used in food preparation, particularly in cereals and potatoes. Research has shown that the reducing sugars are the limiting factors in potatoes, while asparagine is the limiting factor in cereal products (Stadler, 2006).

The Mechanism of Formation

The mechanism for acrylamide formation in starchy foods involves two components of these foods namely reducing sugars and amino acid asparagines (YuZhang *et al*., 2009). The sugars react with asparagines when the food is heated and through a cascade of reactions, the side chain of asparagines is converted to acrylamide (Zyzak *et al*., 2003). These reactions, which produce the brown colour, crust and characteristic tasty flavor of baked, fried and toasted foods (Gokmen and Senyuva, 2007; Mottran *et al.*, 2002).

Heating and time parameters have a direct influence on acrylamide formation in fried potatoes and fried rice (Yu *et al*., 2009). In food, acrylamide is produced in the course of Maillard reaction and its precursors are reducing saccharides and amino acid asparagines (Zhang and Zhang, 2007). Acrylamide formation in food depends on food composition and processing conditions (Zyzak *et al*., 2003). Significant quantities are formed during heat treatment above 120°C, mostly at 150 to 180°C, while at still higher temperatures the extent of formation decreases. The decrease may be explained by the fact that acrylamide as an intermediate product of Maillard reaction (Mikulikova and Sobotovab, 2007).The rate of acrylamide formation increased with temperature, and it was greatest (about 6.06 ppb/s on average) for the potato chips fried at 180°C. Chen *et al*. (2012) recorded that acrylamide levels in fried rice crust and fried potato ranged from 100.46 to 491.76 μg/kg and 58.40 to 4126.26 μg/kg, respectively. It is clear that the acrylamide concentration significantly increased by increasing in temperature at all different times, significant quantities are formed during heat treatment above 100°C specifically at a temperature of 120°C. In the same trend, by increasing frying time, the acrylamide concentration significantly increased at all different temperatures. It is primarily a surface reaction, so that acrylamide in bread is primarily located in the crust with very low or no amounts in the crumb. As temperature increases and moisture content decreases, acrylamide formation increases (Nagao *et al*., 2007) In general, the darker in colour the food product (burnt toast, darker chips), the higher the acrylamide content. Acrylamide appears to form as a byproduct of high-temperature cooking processes (greater than 120°C or 248°F).

In food, acrylamide can be formed in two basic ways. First, acrylamide can be formed when amino acids interact with sugars in the presence of heat. Many different kinds of sugars and many different amino acids can interact in this way. However, one particular amino acid called asparagines has a far greater tendency to interact with sugars and to form acrylamide than other amino acids.

Second, it is possible to form acrylamide without the presence of sugars. When fats in food are oxidized, unique 3-carbon molecules (including acrylic acid and acrolein) can be formed. In the presence of heat, these 3-carbon molecules can interact with asparagine to form acrylamide. It's common for fried foods to form acrylamide in this way, even when there is little sugar found in the foods, no sugar added during frying, and little breakdown of starch into sugar. One noteworthy example of acrylamide formation involves the conventional production of potato chips (Caroline *et al*., 2012). There are small amounts of asparagine present in raw potatoes before processing. During the frying process, fats used for frying can be oxidized and can become converted into acrolein and acrylic acid. Starches in the potato can also be broken down into sugars. This unique mixture of substances can interact in a way that results in unusual amounts of acrylamide formation. Potato chips can commonly contain more than 1,000 parts per billion (ppb) of acrylamide. In a very small, one ounce snack-sized bag of potato chips, this amount would represent about 28 micrograms of acrylamide. In the above example, you'll notice that potato chips can commonly contain more than 1,000 ppb. That's the same as saying that potato chips reach up into the parts per million (ppm) range with respect to their acrylamide content. This high level is unusual. Most foods that contain acrylamide provide it in ppb levels, not ppm levels. Ppm levels are 1,000 times greater than ppb levels. When you consider the overall research on acrylamide in food, the list of foods potentially containing ppm levels is very limited. The percentage contribution of potato products may be even higher for children and adolescents (Dybing *et al*., 2005), partly because this group drinks less or no coffee.

Health – Damaging Properties of Acrylamide

The health impairment caused by acrylamide hinges on its carcinogenic and genotoxic impact (Al-Mosaibih, 2013; Arribas-Lorenzo and Morales, 2012). Acrylamide is a compound, with a potential to cause a spectrum of toxic effects, including neurotoxic effects as has been observed in humans. Exposure to high levels of acrylamide in the workplace have been shown to cause neurological damage, e.g., among workers using acrylamide polymers to clarify water in coal preparation plants.

Acrylamide induces groups of white blood cells to produce free radicals which reduces their cellular glutathione concentration, the consumption of acrylamide containing food products triggers inflammation and oxidative stress which induces atherosclerosis. Glutathione is one of the antioxidants produced in the body (Tareke *et al*., 2000).

Acrylamide Exposure Sources

People who work with materials or processes that use acrylamide can be exposed to it through inhalation, absorption, skin ingestion and skin or eye contact. Consumers can also be exposed to acrylamide through environmental sources, such as water, highly cooked or heat processed foods, tobacco, smoke can be significant source of exposure, and some cosmetics also contain acrylamide.

Still, it is far more likely that the average person will encounter acrylamide in food rather than via water contamination (Spivey, 2010).

Health Risks Associated with Acrylamide

The discovery of acrylamide in food is a concern because it is a well-known industrial chemical whose toxicological properties have been studied extensively. It is a potential human carcinogen and genotoxicant, based on high-dose animal studies, and a known human neurotoxicant (Claudio*et al*., 2006; Katja *et al*., 2008). Acrylamide poses an elevated health risk to children. The acrylamide in foods consumed by pregnant women has been shown to reduce birth weight and head circumference, key indicators of a child's future health. Critically, because of their smaller size and the types of foods they consume, young children are typically exposed to twice as much acrylamide, per kilogram of body weight each day, as adults (Dybing *et al*., 2005),

The International Agency for Cancer Research (IARC) classifies acrylamide as "probably a human carcinogen" based on animal studies (IARC 1994). Acrylamide is genotoxic in a range of assays and is acutely neurotoxic (Hogervorst *et al*., 2009). It is a known human neurotoxin. It is highly likely that exposure from consumption of acrylamide containing food is far below the exposure required for neurotoxicity (Berger *et al*., 2011). However, the primary metabolite of acrylamide is glycidamide, an epoxide that readily reacts with DNA. This raises concerns about potential genotoxicity (Deryck, 2007). However, at this time, insufficient information is available to address carcinogenicity or genotoxicity in humans from the amount of acrylamide consumed in the normal diet. Exposure to acrylamide irritates the nose, throat, and skin; causing a rash or burning feeling on contact. It can lead to loss of balance, slurred speech, and heavy sweating.

Acrylamide triggers "Advanced Glycated End products formation. Advaced glycated end products (AGEs) are toxic substances formed when glucose binds to protein, carbohydrates or fats (Tareke, *et al*., 2002). French fries, potato chips, crackers, and other high-acrylamide foods are often high in calories and low in nutritional value. High consumption of these foods has been linked to increased cancer risk for reasons that have nothing to do with acrylamide. People who eat lots of these foods tend to crowd other foods off the plate. Foods such as vegetables, fruits, beans and whole grains, which have been shown to provide protection against certain types of cancer. Eating a lot of fat and calories also contributes to obesity, which can increase the risk for many cancers.

Foods contributing the most to these exposures will vary between different countries and according to the daily diet. A food or diet item relatively low in acrylamide content, such as coffee or bread, can make a significant contribution to the dietary intake of acrylamide when it is consumed in larger quantities (Becalski *et al*., 2011).

Acrylamide is a food problem, not that of one or a few particular foods. For example, in the US it is estimated that foods containing acrylamide contribute 38% of the daily calories, 33% of the carbohydrates, 36% of the fibre, and more than 25% of a significant number of micronutrients (Petersen and Tran, 2005). This is a very important observation, particularly since so much emphasis is placed on the contribution of crisps and potato chips as sources of acrylamide in normal diets.

Reduction of Acrylamide

The information available on acrylamide reduction reinforces general advice on healthy eating, including moderating consumption of fried and fatty foods (Agnieszka *et a*l.,2004). The addition of antioxidants has been found to prevent acrylamide formation. Antioxidants are substances which inhibit the formation of free radicals in the food and eliminate free radicals in the body. Reduction/mitigation of acrylamide in foods can be approached through removing reactants (fructose, glucose, asparagine) before the heating process, disrupting the reaction (addition of amino acids, food grade acids, changing reaction conditions) and removing acrylamide after its formation during heat processing. The latter approach has not proved to be viable (Parker *et al*. 2012).

Also, it is pertinent to avoid eating a lot of carbohydrate-rich foods that are cooked at high temperatures (e.g. French fries), foods with higher protein content appear to have lower amounts of acrylamide and overcooking foods (Atsushi*et al*., 2014; Granda *et al*., 2004; Xu *et al*., 2014).
It is recommended that people should adhere strictly to the following:

- Continue to eat a balanced diet rich in fruits and vegetables.
- Limit the consumption of fried, fatty, and salty foods.
- Get regular physical activity.
- Maintain a healthful weight.
- Limit the rate of alcoholic intake.
- Avoid smoking.
- Storage of potato tubers at temperatures not lower than 8-12 C
- Avoidance of high (>180-190 C) frying and baking (>250 C) temperatures.

The WHO/FAO consultation advised that food should not be cooked excessively, i.e., for too long a time or at too high a temperature, but also advised that it is important to cook all food thoroughly--particularly meat and meat products--to destroy food borne pathogens (bacteria, viruses, etc.) that might be present. Raw materials with low precursor concentration would generate less acrylamide in any form of cooking, industrial or domestic, and would reduce the need to adapt processes Hence, potato varieties that are low in acrylamide precursors but give desirable sensory attributes when fried or oven baked are keenly sought (Ciesarova*et al*., 2010; Halford *et al*., 2012; Muttucumaru *et al*., 2013; Muttucumaru *et al.*, 2014; Olsson *et al*., 2004).

The acrylamide mechanism in the home is the same as in the industry. This means that an enzyme (asparaginase) could potentially be used to reduce acrylamide in home prepared foods.

This most likely would require producers of ingredients to pre- treat their products rather than having the home maker treat the food.

Furthermore, the rate of acrylamide elimination depends on temperature (faster rates at higher temperatures). Acrylamide content increased with time and temperature of baking, with higher effects perceived at higher temperatures and longer times in an accelerating slope (Casadoa *et al*., 2010; Mustafa *et al*., 2005). Simple soaking and rinsing of potatoes before frying for at least 15 min was found to be very effective in reducing acrylamide up to 63% (Jackson and Al-Taher, 2005). This is attributed to leaching out sugars and asparagine from the surface of potatoes (Ismial *et al*., 2013).

THE MECHANISM OF REDUCTION

N-acetyl- cysteine and lipoic acid have been shown to be protective against acrylamide toxicity and offers a dietary means of counteracting acrylamide's bad effects. N-acetyl-L-cysteine inhibits the incidence of tumors (Banchero *et al.,* 2013)

Once ingested, acrylamide can be detoxified in the body if it is processed through our cytochrome P450 enzyme system and converted into glycidamide, or if it is hooked together with the sulfur-containing, antioxidant molecule called glutathione (Alaattin *et al*., 2012; Daria *et al*., 2013). Even though our metabolic pathways can help us detoxify acrylamide, however, we can still overload the detoxification capability of these pathways and put ourselves at health risk from excess exposure to this substance. The fact that we have detoxification capacity, however, makes it very likely that we can help lower our risk of problems from acrylamide if we have kept plenty of glutathione on hand in our metabolic reserves. One way to help support our glutathione supplies is to consume plenty of sulfur-containing foods (like onions, garlic, and cruciferous vegetables), and especially foods that contain significant amounts of the amino acid cysteine. (Cysteine is one of the key components of glutathione.) Cruciferous vegetables like broccoli and Brussels sprouts, onions, garlic, and red peppers are plant foods that can provide higher-than-average amounts of this amino acid. Poultry, yogurt, and eggs are animal foods that have good concentrations of cysteine.

Ways of Reducing Acrylamide Formation in Meal Preparation

- Cook potatoes to a golden- yellow, not brown.
- Toast bread to the lightest colour possible.
- Heat oil to 145 degrees Celsius- 170 degree Celsius (300 degree F-350degree F) for deep frying foods.
- Always use accurate cooking instructions.
- Read the instructions on the package of pre-fried foods
- Avoid using the microwave especially in cooking starchy foods.

Conclusion

Direct exposure to pure acrylamide by inhalation, skin absorption, or eye contact irritates the exposed mucous membranes and can also cause sweating, urinary incontinence, nausea, myalgia, speech disorders, numbness, paresthesia, and weakened legs and hands. The mutagenic and carcinogenic properties of acrylamide can be strictly reduced, if people could limit their intake of processed foods, fried and fatty foods. Carbohydrates rich food should not be prepared at a temperature higher than 120 degrees Celsius.

Further epidemiological cohort studies are needed to help determine and/ explore the effects of dietary acrylamide intake on human cancer risk. Biospecimen collections in cohort studies will provide an opportunity to avoid the limitations of interview-based dietary assessments by examining biomarkers of exposure to acrylamide and its metabolites in relation to the subsequent risk of cancer. The results of these various studies will help the industry to adopt practical effective and innovative ways to reduce the levels of acrylamide.

The use of acrylamide in foods should not exceed 2% and up to 10mg polyacrylamide, 1L water can be used to wash or peel fruits and vegetables. Ameliorating acrylamide in food products while protecting other quality aspects and reducing dietary acrylamide exposure still remains a major challenge as complete acrylamide removal is probably not possible due to other, minor asparagine- independent formation pathways.

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