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Acrylamide- A Potent Carcinogen in Food

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Abstract: ***Acrylamide is a toxic and potentially carcinogenic chemical. It was assumed that the mechanism leading to the formation of acrylamide derived from Maillard reaction, i.e. the reaction between reducing sugars and proteins/amino acids. Acrylamide is a substance that is produced naturally in foods as a result of high-temperature cooking like baking, grilling, frying etc and it can cause cancer in animals and experts believe it could cause cancer in humans. Acrylamide is a known lethal neurotoxin and animal carcinogen. Acrylamide is genotoxic, therefore acrylamide has the potential to induce heritable damage at gene and chromosome level. There is limited evidence that acrylamide may damage the male reproductive glands. Exposure to acrylamide irritates the nose, throat, and skin, causing a rash or burning feeling on contact. All the above described effects reveals the dangerous effects of acrylamide to humans and it should be controlled in foods.***

Keywords: Acrylamide, food toxin, carcinogen, maillrard reaction, poly-acrylamide

1. Introduction

Acrylamide (or acrylic amide) is a chemical compound with the chemical formula C_3H_5NO. Its IUPAC name is prop-2-enamide. It is a white odourless crystalline solid, soluble in water, ethanol, ether, and chloroform. It is incompatible with acids, bases, oxidizing agents, iron, and iron salts, also it decomposes non-thermally to form ammonia, and thermal decomposition produces carbon monoxide, carbon dioxide, and oxides of nitrogen. Acrylamide is prepared on an industrial scale by the hydrolysis of acrylonitrile by nitrile hydratase. The main uses of acrylamide include the synthesis of polyacrylamides, which find many uses as water-soluble thickeners. These include use in water treatment, gel electrophoresis , papermaking, ore processing, and in the manufacture of permanent press fabrics (USFDA, 2004). Some of them are used in the manufacture of dyes and the manufacture of other monomers.

Acrylamide is a substance that is produced naturally in foods as a result of high-temperature cooking (Tareke et al., 2002). Acrylamide can cause cancer in animals and experts believe it could cause cancer in humans. Although it has probably been part of our diet since man first started cooking, world experts have recommended that we reduce the levels of acrylamide in foods, because of concerns over safety. Acrylamide has been found in a wide variety of cooked foods, including those prepared industrially, in catering and at home. It is found in staple foods such as bread and potatoes as well as in other everyday products such as crisps, biscuits and coffee. Acrylamide is also known for its lethal neurotoxicity (median lethal dose in rabbit = 150mg/kg) and also an animal carcinogen. Its discovery in some cooked starchy foods in 2002 prompted concerns about the carcinogenicity of those foods. AA has been determined in numerous cooked and heat-processed foods in countries, including The Netherlands, Norway, Switzerland, the UK, and the US

(http://www.who.int/foodsafety/publications/chem/acrylamid e faqs/en/index.html).

2. History of Acrylamide

Acrylamide was first synthesized in 1949. Polyacrylamide was first used in laboratory setting in the early 1950s. In 1959, the group of Davis and Ornstein and Raymond and Weintraub independently published on the use of polyacrylamide gel electrophoresis to separate charged molecules. Since then, production of this toxic substance within the European Union has reached approximately 100,000 tonnes per year. It is used almost exclusively in the production of polyacrylamides. Polyacrylamide is used in sewage treatment, in paper and pulp processing, and in the treatment of minerals, and is an additive to cosmetics and paints.

3. Acrylamide in Food

Acrylamide has been found to occur in many cooked starchy foods and is of concern as a possible carcinogen. Acrylamide was accidentally discovered in foods in April 2002 by scientists in Sweden when they found the chemical in starchy foods, such as potato chips, French fries, and bread that had been heated. (USFDA, 2004). It was not found in food that had been boiled or in foods that were not heated. The primary means through which acrylamide is formed in foods is by reaction between asparagine (an amino acid) and reducing sugars such as glucose and fructose. This reaction generally occurs at higher temperatures (Biedermann et al., 2002) and in low moisture conditions, and it is part of the Maillard reaction that provides color, flavor, and aroma in cooked foods. Other formation mechanisms have also been reported; however, the extent of contribution of these mechanisms to total dietary acrylamide levels has not been completely assessed. The alternative mechanisms include production from precursors such as 3-aminopropionamide, acrylic acid, and acrolein, and reactions between other amino acids (e.g. alanine, arginine, cysteine etc.) and other sugars (e.g. galactose, lactose, and sucrose).

Later studies have found acrylamide in black olives, prunes, dried pears and coffee. Estimates for the proportion of acrylamide in adults' diet coming from the consumption of coffee range from twenty to forty percent; prune juice has a high concentration of acrylamide, though adults consume it in far smaller quantities (FAO/WHO, 2002).

3.1 Acrylamide Formation

Potentially toxic acrylamide in foods is largely formed by heat-induced Maillard-type reactions (Kawamura, 1983) between the amino group of the free amino acid asparagine and the carbonyl group of reducing sugars such as glucose and fructose during baking and frying or reactive carbonyls at temperatures above 120°C (Mottram etal 2002). Although sucrose, a non-reducing disaccharide, does not appear to be directly involved in acrylamide formation, it can undergo enzyme-catalyzed conversion to glucose and fructose during cold-storage of potatoes at <10 °C(Carrieri et al., 2009).

3.2 Factors Affecting Acrylamide Formation

The studies shows that starch presence can have an inhibitive effect on the formation of acrylamide. The water content is one of the most important factors in the formation of acrylamide, besides the reaction temperature and time (Slayne and Lineback, 2005 and Gertz and Klostermann, 2003). The minimum of acrylamide formation was observed at the water content between 25 and 40%; outside of this range, the acrylamide concentration was higher. Fructose was more effective for the acrylamide formation in comparison with glucose(Yaylayan et al., 2003). If both glucose and fructose were present in a low-moisture system, the acrylamide yield was not higher than in that containing glucose itself. The water content and the physical state of the food matrix can affect the mechanistic pathway to the acrylamide formation(Amrein et al., 2004). Water impacts the chemical route (e.g. hydrolysis of the imine) as well as the molecular mobility of the chemical constituents which indirectly contributes to the formation of acrylamide (Romani et al. (2009).

3.3 Uses of Acrylamide

The principle use of acrylamide is in water-soluble polymers used as additives for water treatment, enhanced oil recovery, flocculants, paper making aids, thickeners, soil conditioning agents, sewage and waste treatment, ore processing, and permanent-press fabrics. The monomer's use is primarily as a chemical intermediate in the manufacture of the polymer. It is also used in the synthesis of dyes, as a cross-linking agent, in soil conditioning agents, in flocculants, in sewage and waste treatment, in ore processing, in adhesives, in paper and textile coatings, and in permanent press fabrics(http://www.acrylamide-food.org/.) Acrylamide is also used in the synthesis of dyes, in copolymers for contact lenses, and the construction of dam foundations, tunnels, and sewers. The largest use for polyacrylamide is in treating municipal drinking water and waste water. The polymer is also used to remove suspended solids from industrial waste water before discharge, reuse, or disposal (Raloff. 2002).

4. Metabolism and Toxicology

The major metabolite formed via the cytochrome P450 pathway is glycidamide. Species differences in the formation of this metabolite have been observed, with acrylamide converted to glycidamide to a greater extent in the mouse than in the rat, based on urinary metabolites. Once absorbed, acrylamide may be conjugated by glutathione-S transferase (GST) to N-acetyl-S-(3-amino-3-oxopropyl) cysteine or it reacts with cytochrome P450 (CYP450) to produce glycidamide (Tareke et al, 2002) . The major metabolite formed in both rat and mouse is N-acetyl-S-(3-amino-3-oxopropyl) cysteine, accounting for approximately 70% of the urinary metabolites observed in the rat and 40% of those observed in the mouse. Both acrylamide and glycidamide are electrophilic and can form adducts with sulfhydryl groups on hemoglobin and other proteins (Hashimoto and Aldridge 1970). There are limited data regarding the potential for acrylamide to form DNA adducts. When isolated nucleosides were incubated with acrylamide in vitro, the adduct yield and the rate of formation was low. In vivo studies in mice following an oral exposure to 100 mg/kg [^{14}C] acrylamide, radio labeled DNA was found in the tissues examined (Pelucci, C. 2012).

In addition to the carcinogenicity bioassays conducted in rats (Friedman et al, 1995), nonstandard carcinogenicity assays (e.g., mouse skin painting initiation/promotion studies) have been conducted in mice (Tareke et al 2000). Increases in lung tumors were also reported. The neurotoxicity of acrylamide has been extensively studied in various animal models, including rats, mice, monkeys, dogs and cats. In rats exposed via the oral route, single doses of 100 mg/kg were reported to result in alterations in grip strength and motor function. Acrylamide has been evaluated for reproductive toxicity in multigenerational studies in rats and mice and in cross-over breeding studies in rats (Zenick et al., 1986) and mice (Chapin et al., 1995). The results of all the above studies are highly consistent. Acrylamide administered in drinking water or by gavage to rats or mice at doses equal to or greater than 5 mg/kg/day resulted in significant increase in both pre-implantation and post-implantation losses with resulting significant decrease in the number of live pups per litre. Eight dominant lethal studies have been conducted in male rats (Smith et al., 1986; Tyl et al., 2000) and mice (Shelby et al., 1987; Bishop et al, 1991; Adler et al., 2000) by the oral route of administration and in male mice by the intraperitoneal injection and dermal routes (Gutierrez-Espeleta et al., 1992). All studies reported the induction of dominant lethal mutations by acrylamide. In the oral studies, significant decrease in fertility and increase in dominant lethality were observed in the first week postdosing (15 mg/kg/day) up to 4 weeks post-dosing (60 mg/kg/day) (Sublet et al, 1989).

5. Methods for Acrylamide Analysis

A great no of methods have been developed in the past years to quantitatively analyse the acrylamide monomer, especially in sugar, field crops and mushrooms. The majority are classical methods based on LC-MS/MS or GC technique. However because of the complexity of food matrices, these methods do not suffice for the analysis of acrylamide in heat treated foods at trace levels. Particularly, they lack selectivity and the additional degree of analyte certainty required to confirm the presence of a small molecule, such as acrylamide in a complex food matrix. Gas chromatography (GC) - mass spectrometry (MS) and HPLC analysis are both acknowledged as the major useful and authoritative methods for the acrylamide determination. Two in-line pre-concentration capillary zone electrophoresis sample injection (CZE) methods namely field amplified sample injection (FASI) and stacking with sample matrix removal (LVSS) have been evaluated for the analysis of acrylamide in food stuff. Due to the lower detection limits obtained with FASI-CZE, this method was applied to the analysis of acrylamide in different food stuff such as biscuits, cereals, crisp bread, snacks and coffee (Summa et al., 2007). A method using normal phase high performance liquid chromatography (NP-HPLC) with UV detection was developed for the analysis of acrylamide. Zhao et al 2005) A simple and rapid method was developed and validated for determination of acrylamide in potato and cereal based foods by using a single quadrapole LC-MS interfaced with positive atmospheric pressure chemical ionization (APCI+). (Kim et al., 2005). A reverse-phase LC-MS based on stable isotope dilution assay was used for acrylamide analysis. A new voltametric biosensor was developed to detect acrylamide in food sample. The interaction between α-NH_2 group of N-terminal Valine of Heamoglobin to form Hb adduct is the basis of this method. This is suitable for the direct determination of acrylamide in food sample (Krajewska et al, 2008).

6. Summary

As acrylamide is a poten toxic substance found in food items, its levels should be monitored and minimized. Also necessary actions to be taken for fixing maximum limits for the acrylamide in commercially available foods.

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