Food and Chemical Toxicology 69 (2014) 1–12

Contents lists available at ScienceDirect

Food and Chemical Toxicology

journal homepage: www.elsevier.com/locate/foodchemtox

Review

Risk assessment, formation, and mitigation of dietary acrylamide: Current status and future prospects

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ARTICLE INFO

Article history:
Received 11 December 2013
Accepted 28 March 2014
Available online 5 April 2014

Keywords:
Dietary acrylamide
Epidemiology
Maillard reaction
Omics
Risk analysis
Toxicology

ABSTRACT

Acrylamide (AA) was firstly detected in food in 2002, and since then, studies on AA analysis, occurrence, formation, toxicity, risk assessment and mitigation have been extensively carried out, which have greatly advanced understanding of this particular biohazard at both academic and industrial levels. There is considerable variation in the levels of AA in different foods and different brands of the same food; therefore, so far, a general upper limit for AA in food is not available. In addition, the link of dietary AA to human cancer is still under debate, although AA has been known as a potential cause of various toxic effects including carcinogenic effects in experimental animals. Furthermore, the oxidized metabolite of AA, glycidamide (GA), is more toxic than AA. Both AA and GA can form adducts with protein, DNA, and hemoglobin, and some of those adducts can serve as biomarkers for AA exposure; their potential roles in the linking of AA to human cancer, reproductive defects or other diseases, however, are unclear. This review addresses the state-of-the-art understanding of AA, focusing on risk assessment, mechanism of formation and strategies of mitigation in foods. The potential application of omics to AA risk assessment is also discussed.

Contents

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http://dx.doi.org/10.1016/j.fct.2014.03.037
0278-6915/

1. Introduction

Acrylamide (AA) is an important industrial chemical, which has been widely used as a flocculating agent in water treatment, as an ingredient in several cosmetic formulations and as a chemical reagent in molecular biology research (Blank, 2005; Friedman, 2003; Pedreschi et al., 2014). It comes to public and academic attention because of its hazards to humans and animals. The Swedish National Food Administration and the University of Stockholm reported that AA is present in many commonly consumed foods, such as bread, fried foods, and coffee (Rosén and Hellenäs, 2002). Interestingly, no AA was found in raw and boiled foods, indicating that AA formation is associated with food processing. Subsequent studies found that AA is formed in food during high-temperature processing, such as cooking, frying, roasting and baking of carbohydrate-rich foods, through a reaction known as the Maillard reaction between sugars and amino acid asparagine, under low moisture conditions (Mottram et al., 2002; Stadler et al., 2002; Tareke et al., 2002; Yaylayan et al., 2003; Zyzak et al., 2003). The Maillard reaction is responsible for the golden color and tasty flavor of baked, fried and toasted foods, and in this sense, AA formation is an adverse by-product of Maillard reaction.

Due to its genotoxicity and carcinogenicity, AA was classified as a Group 2A carcinogen by the International Agency for Research on Cancer (IARC, 1994) and a Category 2 carcinogen and Category 2 mutagen by the European Union (EC, 2002), which caused worldwide concern (FAO/WHO, 2002). It was put into the list of substances of "very high concern" by the European Chemical Agency in 2010. Therefore, the food industry faces a challenge to modify the processes or to change the product parameters without compromising the quality of their foods. This depends largely on a better understanding of AA formation and mitigation technologies, and toxicological mechanisms as well.

During the past years, many new epidemiological studies have been carried out to investigate the association of dietary AA or occupational AA exposure with cancer in humans (Bongers et al., 2012; Chen et al., 2012; Erdreich and Friedman, 2004; Hogervorst et al., 2007, 2014; Konings et al., 2010; Larsson et al., 2009; Lujan-Barroso et al., 2014; Wilson et al., 2010). These studies have been summarized in several extensive reviews (Pelucchi et al., 2011, 2014; Lipworth et al., 2013, 2012). So far, epidemiological studies do not suggest a clear association of cancer with dietary or occupational exposure to AA. Therefore, novel epidemiological studies using large populations with broad exposure contrasts and biomarkers of human diseases include cancers are needed.

The review addresses some critical issues of AA with a focus on risk assessment, formation mechanisms and mitigation technologies. The prospects of AA risk assessment are discussed as well.

2. AA formation

To control the formation of this potential carcinogen in food, detailed knowledge of its mechanism of formation is of critical importance. So far, there are at least a major pathway and a minor pathway for AA formation. Some critical and direct precursors contributing to the formation of AA include 3-aminopropionamide (3-APA), decarboxylated Schiff base (Zyzak et al., 2003), decarboxylated Amadori product (Yaylayan et al., 2003), acrylic acid (Becalski et al., 2003; Stadler, 2003; Stadler et al., 2003), and acrolein (Yasuhara et al., 2003), all of which, together with factors affecting AA formation will be briefly summarized in following sections.

2.1. Major AA formation pathway

The major pathway for AA formation in food is known as the asparagine route via Maillard reaction (Mottram et al., 2002; Stadler et al., 2002; Tareke et al., 2002; Yaylayan et al., 2003; Zyzak et al., 2003). In this *N*-glucosides route, asparagine is converted to AA through thermal decarboxylation and deamination, which necessarily needs the presence of a carboxyl compound (such as a reducing sugar) (Granvogl and Schieberle, 2006; Stadler et al., 2004). In model studies, α-hydroxy carbonyl is more effective than di-carbonyls in converting asparagine to AA (Stadler et al., 2003), and fructose, which contains two α-hydroxy carbonyl groups, increases AA formation by about 2-fold compared with other reducing sugars such as glucose (Eriksson, 2005; Granvogl et al., 2004; Stadler et al., 2002, 2003, 2004; Yaylayan et al., 2003). In this pathway, the reaction between asparagine and a reducing sugar yields a decarboxylated Schiff base, *N*-glycosylasparagine, which leads directly to AA and an imine after decomposition. In addition, decarboxylases present in the raw materials might generate the biogenic amine 3-APA from asparagine, which is then thermally deaminated into AA. This process proceeds without involving reducing carbohydrates.

Strecker degradation of amino acids (asparagine and methionine) in the presence of reactive di-carbonyl products to aldehydes, the Strecker aldehyde route, has been suggested as an alternative way of AA formation via Maillard reaction (Mottram et al., 2002; Stadler et al., 2004). The important steps and intermediates of the major AA formation pathway are shown in Fig. 1A.