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What Makes Acrylamide Dangerous

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Abstract
Acrylamide, commonly used in various industries, is firstly known as a neurotoxicant. In 1994, acrylamide was categorized in Group 2A, which are probably carcinogenic substances. In 2002, acrylamide was discovered to form in foods. Later, its effects on many organs were detected. Among them, acrylamide and its byproduct glycidamide were also found as a strong reprotoxic agent due to its binding capacity to biologically important molecules, including DNA and protein. Although carcinogenicity of acrylamide was not proved in humans, acrylamide has been proved to lead to various cancer types in animal studies. However, in our experiments and in a few papers, low dose acrylamide was reported to increase proliferation in commercial cells. Even though acrylamide did not lead to cancer in humans, it poses a risk for augmenting the malignancy of the cells. The proliferating effect of acrylamide is required to be explored more extensively. In conclusion, acrylamide is a toxic agent we expose even in our daily foods in our homes. The fact that it binds DNA and macromolecules, is a neurotoxicant and reprotoxic agent, and categorized in probably carcinogenic agents is sufficiently convincing evidence to implement some regulations to restrict its amount.
Keywords: *Acrylamide, Food, Neurotoxicity, Reprotoxicity, Cancer*.

Introduction

Acrylamide is the chemical that was synthetically produced in the years of 1950s. It has been utilized in many industrial sectors for various purposes since. In the industrial workers, some neurology-related health problems were observed, leading the neurotoxicity of acrylamide to be found. In 1994, acrylamide was categorized in Group 2A, which are probably carcinogenic substances, by International Agency for Research on Cancer (IARC). Who could have known that acrylamide had already existed and most of us had exposed it in our daily diet? In 2002, acrylamide was discovered to form in foods by a chemical reaction called Maillard. This formation needs some special requirements. The more these requirements are met, the more acrylamide forms. First, the temperature must be higher than 120°C. The processed foods including more carbohydrate and less protein, but higher amino acid asparagine show a tendency to produce higher acrylamide content. And more importantly, the process types grilling, roasting, frying, etc. are the major factors to lead to acrylamide formation. Acrylamide was first known as a neurotoxicant and then added to probably carcinogenic substances; later its effect on multiple body systems was studied. Among them, acrylamide was also found as a strong reprotoxic agent due to its binding capacity to biologically important molecules, including DNA and protein. What's more, in the acrylamide clearance stages in the body, a more toxic agent, glycidamide was forming. Glycidamide, as a byproduct of acrylamide, was reported to have at least 100-fold more propensity to bind DNA than that of

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acrylamide. As for acrylamide being Group 2A substance, although in animal studies acrylamide has been proved to lead to various cancer types, in human-related studies there is no unanimity and it is still in the air. There are different controversial reports. However, in our experiments and in a few papers, low-dose acrylamide was reported to increase proliferation in commercial cells. Even though acrylamide did not lead to cancer in humans, it might exacerbate or increase the tendency of malignant cells to induce cancer. The proliferating effect of acrylamide is needed to be focused more comprehensively.

In this review, we summarized the toxicity of acrylamide with terms of neurotoxicity, carcinogenicity, reprotoxicity and other organ toxicity. In the end, we will finalize our review by mentioning its potential proliferative effect on cells.

What makes acrylamide dangerous?

We summarized the toxicity of acrylamide in five categories: neurotoxicity, carcinogenicity, reprotoxicity, other organ toxicity and its potential proliferating effect.

a.Neurotoxicity of acrylamide

He et al. (1989) conducted a study over the workers in the factories manufacturing acrylamide and detected neurodegenerative signs, such as weakness in legs, loss of the reflex and feeling of toes and heel, and numbness in the hands (He et al., 1989). The workers exposed to acrylamide exhibit signs of peripheral neuropathy(Calleman, Bergmark, Stern, & Costa, 1993; Costa, 1996; Gerrard, 2006). Lon-term acrylamide exposure was reported to lead to cerebellar dysfunction apart from peripheral neuropathy (He et al., 1989). In another study, the NOAEL (No Observed Adverse Effect Level) value for the peripheral neuropathy that is induced by acrylamide-containing drinking water was found 0.5 mg/kg daily. Besides, higher amounts of acrylamide were contended to engender neuropathy in the central nervous system (Tritscher, 2004).

b. Carcinogenicity of acrylamide

In 1994, the International Cancer Research Institute (IARC) included acrylamide in the Group 2A substances, which are probably cancerogenic in humans (IARC, 1994). Acrylamide was reported to cause cancer in many organs in animals studies (Dabrio et al., 2008; Halford, Curtis, Muttucumaru, Postles, & Mottram, 2011; Sharp, 2003; Tsutsumiuchi et al., 2004; Wakaizumi, Yamamoto, Fujimoto, & Ozeki, 2009). In long-term exposure, acrylamide was demonstrated to augment peritesticular mesothelioma, follicular adenoma in the thyroid, clitoral gland adenomas, oral cavity papillomas and glial tumors (Friedman, Dulak, & Stedham, 1995; Johnson et al., 1986). In toxicological studies in mice and rats, feeding of animals with acrylamide-containing food poses risk for the lung, mammary gland, oral cavity and intestine cancers (Galeša, Bren, Kranjc, & Mavri, 2008; Mucci, Dickman, Steineck, Adami, & Augustsson, 2003; Rice, 2005). In addition, acrylamide is stated to cause skin cancer when in contact with skin and lung cancer when inhaled (Rice, 2005).

c. Reprotoxicity of acrylamide

Regarding the effects on reproductivity, acrylamide causes a decrease in sperm count and an increase in abnormal sperm morphology and vacuolizations in spermatogenic cells (Sakamoto & Hashimoto, 1986). It gives rise to DNA damage during the process of spermatogenesis (Sega, Generoso, Brimer, & Malling, 1990). Acrylamide damages Leydig cells and reduces testosterone levels (Yang et al., 2005a). Acrylamide causes multi-nucleated giant cells and an increase in vacuolization in the seminiferous tubules, sperm abnormalities and leads testicular cells to apoptosis. Male mice treated with were reported to show a reduction in mating, productivity, pregnancy and even sperm transport (Tyl, Marr, Myers, Ross, & Friedman, 2000). Also, Gassner and Adler (1996) point out that acrylamide delays cell cycle (Gassner & Adler,

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1996). Acrylamide was found to induce spermatid mutations in mice and rats. Therefore, acrylamide is thought to be a mammalian reproductive cell mutagen (Adler, Schmid, & Baumgartner, 2002; Shelby, Cain, Cornett, & Generoso, 1987). Acrylamide reduces testicular weight (Reddy, Rani, Sainath, Meena, & Supriya, 2011; Wang et al., 2010).

d. Other organ toxicity of acrylamide

Although not as much and common as the studies related to nervous and reproductive systems, the toxicity of acrylamide was investigated in other organs, including ovarium, liver, lung, kidney, heart, stomach, intestine and spleen. In those studies, acrylamide was also reported to exert toxicity in these organs. (Kacar & Sahinturk, 2018).

e. Does acrylamide proliferate cells at low concentrations?

In the cytotoxicity test in our laboratory (unpublished), we observed proliferative trends in some type of cells at low acrylamide doses despite the toxicity of high acrylamide doses. In our literature search, we also accessed two similar reports in HepG2 cell line. The lower doses (≤100 μM) of acrylamide augmented the proliferation of this cell line (Shan et al., 2014; Xu, Wang, Xu, Shan, & Feng, 2019). Given that the same low dose acrylamide does not proliferate all cell types but the certain ones, it is more conceivable to say that acrylamide displays different effects according to the cell type.

Conclusion

To recap, acrylamide is a chemical we expose even in our daily foods in our homes. The fact that it binds DNA and macromolecules, neurotoxicant, reprotoxic agent and categorized in probably carcinogenic agents is sufficiently persuading evidence to introduce some regulations to restrict its content.

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