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Innovation The Research Concept

Acrylamide:Toxicity and Carcinogenicity in Foods

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Abstract

Acrylamide (AA) is a naturally occurring, widely used compound, it is produced during high temperature processing of food by cooking, frying, toasting, roasting or baking of carbohydrate rich foods. Ingestion of large amounts of Acrylamide underlies several health concerns as Neurotoxicity, reproductive toxicity and immunotoxicity. Acrylamide (or acrylic amide) is an organic with the chemical formula CH_2=CHC(O)NH_2.. It is a white odorless solid, soluble in water and several organic solvents. It is produced industrially as a precursor to polyacrylamides,which find many uses as water-soluble thickeners and flocculations agents. It is highly toxic,likely to be carcinogenic and partly for that reason it is mainly handled as an aqueous solution.

Some cooked foods contain acrylamide attracted significant attention to its possible effects.[1] EPA,NTP and IARC has classified it as a probable carcinogen. Although epidemiological studies suggests that dietary acrylamide consumption does not significantly increase people's risk of developing cancer genomic analysis has revealed widespread contribution of acrylamide exposure to human carcinogenesis.

Keyword: Acrylamide, toxicity, food, carcinogen.

Introduction

Ea(or acrylic amide) is an organic with the chemical formula CH_2=CHC(O)NH_2.. It is a white odorless solid, soluble in water and some polar solvent like ethanol,methanol and acetone. This substance is formed during the preparation of some foods at a high temperature of more than 125 degrees Celsius, by roasting for some types of foods that have a high percentage of carbohydrates such as potato chips, toast, etc Zamani et al.[2]It was discovered and classified as pollutants in 2002 by the Swedish National Welfare Food Committee Fang et al.[3] AA can also be exposed in the environment or workplaces through air and water, and during its production or use, in addition to its presence in adhesives, cosmetics, and graphic films Taeymans et al.[4] Many occupational and environmental problems have been registered from the wide use of AA which was primarily used as flocculants for clarifying drinking water Granath et al.[5] Indeed, AA is used mainly in the formation of poly-acrylamides, which are widely used in plastics, paints, varnishes, adhesives and mortar. It is also applied in toiletries and cosmetics Pingot et al.[6] Naturally, AA is formed through interaction of amino acids with reducing sugar. This occurs during frying, grilling, baking or roasting carbohydrate rich food as bread, potato crisps, chips crackers and french fries at temperatures above 120^{0}C. This increased the concern about cancer risks associated with the dietary intake of fried or backed carbohydrate food. It was evident that exposure to large doses of AA causes damage to male reproductive glands. Adding to this, direct AA inhalation or skin absorption irritates the exposed tissue and can lead to nausea, sweating, speech disorders, paresthesia, numbness, myalgia, urinary incontinence and paraparesis Alberts et al.[7]. It is produced industrially as a precursor to polyacrylamides,which find many uses as water-soluble thickeners and flocculations agents. It is highly toxic,likely to be carcinogenic and partly for that reason it is mainly handled as an aqueous solution.

Acrylamide

Names	
Preferred IUPAC name Prop-2-enamide[2]	
Other names Acrylamide Acrylic amide[2]	
Properties	
Chemical formula	C_3H_5NO
Molar mass	71.079 g·mol⁻¹
Appearance	white crystalline solid, no odor[2]
Density	1.322 g/cm³
Melting point	84.5 °C (184.1 °F; 357.6 K)
Boiling point	None (polymerization); decomposes at 175–300 °C[2]
Solubility in water	390 g/L (25 °C)[2]
Hazard	Carcinogenic

Risk of Acrylamide in food

Since acrylamide is present in a wide range of everyday foods,this to all human being but children are the most exposed age group on a body weight basis Possible harmful effects of acrylamide on the nervous system, pre- and post-natal development and male reproduction were not considered to be a concern, based on current levels of dietary exposure.

The most important food groups contributing to acrylamide exposure are fried potato products,coffee, biscuits, crackers and crisp breads and soft bread.

The ingredients, storage and processing conditions(particularly temperature) greatly influence acrylamide formation in food.

What happens to acrylamide in the body

Following ingestion, acrylamide is absorbed from the gastrointestinal tract,distributed to all organs and extensively metabolised, Glycidamide is one of the main metabolites resulting from this process.

Laboratory animals orally exposed to acrylamide have an increased likelihood of developing gene mutations and tumours(among others, in rats- mammary gland, testes and thyroid gland; and in mice- Harderian and mammary glands, lung, ovaries, skin and stomach). Glycidamide is the most likely cause of these types of adverse effects in animals. Acrylamide exposure can also lead to harmful effects on the nervous system(including hind limb paralysis), pre-and post-natal development and adversely affect male reproduction.

Result from human studies provide limited and inconsistent evidence of increased risk of developing cancer (of the kidney, endometrium and ovaries)in association with dietary exposure to acrylamide.

Dietary Exposure

The presence of acrylamide in heat processed food is a worldwide health concern, since this substance has been classified as a probable human carcinogen by the International Agency for Research on Cancer(ICAR)[8.] Acrylamide is primarily formed in food products derived from raw materials that are rich in carbohydrates and low in proteins.[9] Fried, deep-fried, or baked food items, such as cake, bread, French fries, and chips are believed to contain the highest levels of acrylamide as shown in Table1. Despite the fact that acrylamide concentration in coffee is relatively low, it is a major contributor to acrylamide exposure in adults because of the high amounts of coffee consumed.[11] Estimates of the average intake of AA by consumers may differ between countries and according to dietary habits, but an average mean intake can be considered to be about 0.4 mg/kg body weight per day (bw/d), and the average intake for a high-level consumer to be about 1.0 µg/kg bw/d.[12] Other researchers estimated the acceptable daily intake to be 1µg/AA/d, which is an amount exceeded in many regular food products.[13] The WHO states that AA has no reliably identifiable threshold of effects, meaning that exposure to low doses might be followed by a symptom silent period in which the detrimental effects of the chemical may not be clinically apparent, but nevertheless morphological and/or biochemical alterations may be present.[14] Tolerable daily intake for neurotoxicity from AA was estimated to be 40 µg/kg/d while that for cancer was estimated to be 2.6 and 16 µg/kg/d based on

AA or glycidamide, respectively.[15] In a study done in , the daily consumption of AA from potato and corn chips was found to be 7- to 40-fold higher

than the risk intake set by WHO but was below the neurotoxic risk threshold. The cancer risk for the population from AA exposure estimations appears to be significant, highlighting the need to conduct further epidemiological studies and to ensure monitoring of AA levels in food products. [16]

Another study on the amount of AA in caffeinated beverages showed that caffeinated beverages contributed an average of 29,176 µg/kg of AA, which was higher than the risk intake for carcinogenicity and neurotoxicity set by the WHO.[17] This study shows alarming results that call for the need to regulate the caffeinated product industry in Lebanon by setting legislations and standard protocols for product preparation in order to limit the AA content and protect the consumers. The Joint Expert Committee on Food Additives had reported that the major foods contributing to the total AA intake for most countries are potato crisps (6%-46%), potato chips (16%-30%), coffee (13%-39%), pastry and sweet biscuits (10%-20%), and bread (10%-30%).[18] Furthermore, food packages that contain polyacrylamide may lead to indirect exposure to AA monomer residual.[19] Although nonfood exposures may exist, the diet is assumed

to be the major source of AA exposure for the general nonsmoking population, where around 38% of caloric uptake is provided by food sources that are known to contain AA.[20].

Table 1. Acrylamide Level in Selected Food Groups

Food Goups	Food prodcut group	Minimum Acrylamide µg/kg	Maximum acrylamide µg/kg
Potatoes	Potato crisps Chips/French fries Potatoes (raw)	117 59 <10	3,770 5,200 <50
Cereal products	Corn crisps Bakery products and biscuits Gingerbread Bread Bread (toast) Breakfast cereals	120 18 <20 <10 25 11	220 3,324 3,324 130 1,430 1,057
Rice and noodles	Fried noodles Fried rice Rice crackers, grilled, or fried	3 <3 17	581 67 500
Fruits and vegetables	Canned black olives Prune juice Fried vegetables	123 53 34	1,925 267 34
Nuts	Nuts	28	339
Fish and meat	Fish and seafood products, crumbed, or battered Meat/poultry products,crumbed, or battered	<2 <10	39 64
Cocoa-based products	Chocolate products Cocoa powder	<2 <10	826 909
Coffee	Coffee (roasted) Coffee substitute Coffee extract/powder	45 116 195	975 5,399 4948

Adapted from Food and Agriculture Organization/World Health Organization.[10]

Objective of the Study

The aim of this study is to determine levels of acrylamide in food acquired from vending machines. Acrylamide in food potentially increases the risk of developing cancer for all age groups.

Absorption, Metabolism, DistributionAnd Excretion

Absorption

Acrylamide is absorbed from all routes of exposure. While data on the bioavailability from food matrices are limited, absorption is considered to be rapid and complete by the oral route in all species.

Metabolism and distribution

Animal studies have shown that acrylamide and glycidamide are widely distributed in all tissues of the body, including milk. The major metabolite of acrylamide, glycidamide, is an epoxide that may be more critical for carcinogenic and genotoxic properties in animals than the parent compound. Acrylamide, rather than glycidamide, probably accounts for its neurotoxic potential.

The major metabolic pathway for acrylamide is qualitatively similar in humans and laboratory animals, however, quantitative differences must be considered in assessing risk for humans. For the range of doses used in animal toxicology studies, the extent of conversion of parent compound to glycidamide is inversely related to the amount of acrylamide in the body – the lower the dose, the higher the proportion converted to glycidamide. Because metabolism and elimination involve pathways where there is

genetic variability (e.g. conjugation and P450- mediated metabolism), there may be variation in the sensitivity of humans to the effects of ingested acrylamide.

Excretion

The elimination half-life of acrylamide and glycidamide is about two hours in rats.

Pharmacokinetic data in humans are sparse.

Neurotoxicity is the only recognized adverse effect of oral acrylamide exposure in humans.Animal studies and human experience demonstrate that acrylamide is neurotoxic throughout postnatal life. Dysfunction of the central nervous system, especially the brain, dominates the acute toxic response to large single exposures. Brain dysfunction may present as seizures (overt poisoning only), or after prolonged exposure, in the form of sleepiness, changes in emotion and memory, hallucination, and tremor. These manifestations of acrylamide intoxication may precede and/or accompany signs of peripheral neuropathy (stocking-and-glove distribution of sensory loss, sweating, and muscle weakness) with or without the ataxia that characteristically results from repeated lower-level exposures to acrylamide. Peripheral neuropathy is a delayed response to acrylamide exposure and, depending on the dose received, may appear within weeks or months of daily exposures to small amounts, and up to several years in the event of chronic, low-level exposures. Rodent studies indicate

that peripheral neuropathy develops more rapidly, and has greater severity and slower recovery in older versus young animals. Neurotoxicity is replicated in animal studies. Less is known about the effects of acrylamide on the developing nervous system, although major persistent structural or functional perturbations of the brain or behaviour resulting from in utero or post-natal exposure have not been found in animal studies. Animal studies demonstrate that acrylamide damages the testes

and adversely affects fertility. Acrylamide is genotoxic in vivo in somatic cells and germ cells, and therefore has the potential to induce heritable damage at gene and chromosome level..

Toxicity of Acrylamide

Neurotoxicity

Neurotoxicity is a major consequence of AA exposure, and considerable attention has been drawn to this area of investigation. This compound is considered to be a cumulative neurotoxicant in rodents as well as in humans.46 In rodent toxicity

studies, exposure to repeated doses of 10 to 50 µg/kg bw/d AA had been reported to cause neuropathy in most laboratory animal species, while exposure to single doses of 100 to 200 µg/kg was fatal in most animals.[21] In vitro, AA was shown to

induce apoptosis in rat primary astrocytes and cause mitochondrial dysfunction and apoptosis in BV-2 microglial cells.[22] Moreover, Chen and Chou showed that AA disrupted the nervous system by inhibiting human neuroblastoma and glioblas toma cellular differentiation.[23] Acrylamide neurotoxicity in occupationally exposed populations has been ascertained by various epidemiological studies.[24] General symptoms of neurotoxicity in humans are a characteristic ataxia, skeletal muscle weakness, weight loss, distal swelling, and degeneration of axons in the central and

peripheral nervous systems.[25]

Genotoxicity and Carcinogenicity

The genotoxicity of AA and its major metabolite glycidamide had been investigated in several studies. A study by Alzahrani in mice showed that single doses of AA at 10, 20, and 30 µg/kg and repeated doses of 10 µg/kg for 1 and 2 weeks significantly

induced DNA damage compared to the control group as shown by elevation in micronuclei and chromosome aberrations in mice bone marrow cells.[26] Moreover, prolonged exposure of animals to high concentrations of AA in the drinking water leads to tumor development at multiple sites in both male and female genders.[27]

Based on the current research, AA is currently classified as a “probable human carcinogen” by the IARC and as “reasonably anticipated to be a human carcinogen” by the US National Toxicology Program.Few researchers have found some association between AA-hemoglobin adduct levels and incidence of estrogen receptor-positive breast cancer as well as between AA intake and endometrial and ovarian tumors in postmenopausal women.

Reproductive Toxicity

Reproductive toxicity of AA in humans has not been demonstrated; however, in rats, the No-observed adverse effect level for reproductive toxicity was assessed to be 2 to 5 μg/kg/d. The administration of 0.5 to 10 μg/kg of AA caused growth retardation in rats and reduction in epididymal sperm reserves compared to the control group.[27] In addition, repeated injections of AA (20 μg/kg) to male rats for 20 days caused decrease in testosterone and prolactin concentrations in a dose-dependent manner. In another study, reproductive toxicity was also revealed in AA-treated female mice, where a decline in the viability of mouse granulosa cells, the number of corpora lutea, and progesterone production was observed.[28]

Hepatotoxicity

Although AA is metabolized in the liver, reports of its hepatotoxicity in humans are still scarce. However, numerous studies in animals have reported the harmful effects of dietary AA in the liver due to oxidative stress. A high dose of 25 μg/kg AA administered for 21 days resulted in significant decrease in liver GSH level and total antioxidant status in experimental adult rats. Administration of AA also led to increase in serum level of liver enzymes (AST, ALT, and ALK) and decrease in

superoxide dismutase and catalase activities, while total oxidant status and malondialdehyde levels increased.[29]

Immunotoxicity

Studies regarding the adverse effects of AA on the immune system are limited compared to other end points. Nevertheless, immunotoxicity of AA was found in female BALB/c mice, where AA decreased final bw, spleen, and thymus weights, and lymphocyte counts in addition to causing pathological changes in lymph glands, thymus, and spleen.[30] Acrylamide was also shown to cross the placenta and reach the fetus, but no significant associations were found between prenatal dietary exposure to AA and the investigated immune-related health outcomes or blood parameters at any age.

Ways to reduce acrylamide in food

Comparing frying, roasting, and baking potatoes, frying causes the highest acrylamide formation. Roasting potato pieces causes less acrylamide formation, followed by baking whole potatoes. Boiling potatoes and microwaving whole potatoes with skin on to make “microwaved baked potatoes” does not produce acrylamide.[Based on FDA studies.]

Soaking raw potato slices in water for 15-30 minutes before frying or roasting helps reduce acrylamide formation during cooking. (Soaked potatoes should be drained and blotted dry before cooking to prevent splattering or fires.)

Storing potatoes in the refrigerator can result in increased acrylamide during cooking. Therefore, store potatoes outside the refrigerator, preferably in a dark, cool place, such as a closet or a pantry, to prevent sprouting.

Generally, more acrylamide accumulates when cooking is done for longer periods or at higher temperatures. Cooking cut potato products, such as frozen French fries or potato slices, to a golden yellow color rather than a brown color helps reduce acrylamide formation (see Picture A). Brown areas tend to contain more acrylamide.

Toasting bread to a light brown color, rather than a dark brown color, lowers the amount of acrylamide (see Picture B). Very brown areas should be avoided, since they contain the most acrylamide.

Acrylamide forms in coffee when coffee beans are roasted, not when coffee is brewed at home or in a restaurant. So far, scientists have not found good ways to reduce acrylamide formation in coffee.

Conclusion

Acrylamide is formed when some foods are cooked or processed at high temperatures. It seems to arise when different food components react together. These may be carbohydrates, proteins and amino acids, lipids, and possibly other minor food components also. The reaction is promoted by heating and increases with the time of heating. It is not yet clear what combinations of food components are involved and it may well be that the situation is complex with many mechanisms operating. The situation is further complicated by the fact that acrylamide is a volatile and reactive substance that could itself be partially lost after formation The.processing and cooking conditions to be optimised to minimize and possibly eliminate acrylamide levels in heated foods.

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