Toxic impacts of Acrylamide: A Review
Jayanti Jatav and *Habiba Bano

Department of Zoology, University of Rajasthan, JAIPUR-302004 (RAJ) INDIA
*Corresponding Author
E-mail: banohabiba@gmail.com

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ABSTRACT
Acrylamide, a harmful chemical produced during the cooking methods, particularly when certain carbohydrate-rich foods are fried, toasted, roasted or baked at high temperatures, has become a major health concern in recent years. It is most prevalent in roasted almonds, French fries and potato crisps, especially when the amino acid asparagine is free and reacts with fructose and glucose sugars. It has been reported to cause alarming health problems due to its widespread consumption, predominantly among the younger generation, which prefers processed and baked foods these days. The current review focuses on various toxic effects of acrylamide such as neurotoxicity, carcinogenicity, genotoxicity, reproductive toxicity, immunotoxicity, hepatotoxicity, cardiotoxicity, hematotoxicity, nephrotoxicity, developmental toxicity including many others.

Figures: 03 References: 63 Table: 00

KEY WORDS: Acrylamide, Food, Human, Toxicity

Introduction
People have been using heat to prepare their foodstuff for thousands of years. Thermal processing is necessary for nutritional quality, microbiological safety, and desired sensory characteristics; nevertheless, undesired substances have emerged as a result of food processing methods. Acrylamide is one such water-soluble molecule that is liberated as a monomer, in carbohydrates-rich foods during the cooking process at high temperatures. Asparagine reacts with glucose to produce a product that gives food its color and flavor. This is called the Maillard reaction, and it occurs at higher rates when the temperature exceeds 120°C. Acrylamide is found in a variety of foods, including bakery products, breakfast cereals, cappuccino powder, roasted coffee, biscuits, wafers cookies, potato chips, fried potatoes, French fries etc. Besides this, it also has a wide range of applications in a variety of industries. Acrylamide has been known as an industrial chemical compound that was primarily utilized in various industrial systems, such as plastics manufacturing, paper and glue production, processing of waste water and drinking water, as well as in the treatment of sewage.

Several studies employing human cells have revealed that prolonged low-level exposure to acrylamide can cause central and peripheral nervous system deterioration with motor and cognitive impairments. According to animal studies, acrylamide causes nephrotoxicity, developmental toxicity, hepatotoxicity, carcinogenicity, neurotoxicity, genotoxicity, reproductive toxicity, with neurotoxicity being the most common.

Neurotoxicity
Acrylamide has been considered to be a potential neurotoxin to human beings according to the reports of the World Health Organization. An effect of acrylamide neurotoxicity has been demonstrated in both occupationally exposed humans and animals. The lowest observed effect limit (LOEL) for neurotoxicity in laboratory animals is 2g/kg/day, and no observed effect limit (NOEL) is 0.2 to 0.5 g/kg/day, respectively. Repeated daily exposure to acrylamide causes skeletal muscle weakness, hind-limb foot splay, and ataxia in a variety of laboratory animals, including mice, rats, cats, monkeys, rabbits, and guinea pigs. Under in vitro conditions, Apoptosis and mitochondrial dysfunction have been observed in BV-2 microglial cells, as well as in rat primary astrocytes exposed to acrylamide.

Acrylamide is found in breast milk and a significant amount of it is passed through the placenta to the developing foetus. Its exposure causes dopaminergic neurodegeneration and alpha-synuclein accumulation, which eventually leads to Parkinson’s disease pathology. Several studies have examined the neurotoxic effects of acrylamide as it is used in the workplace.
Carcinogenicity and Genotoxicity

The International Agency for Research on Cancer (IARC) has classified acrylamide as potentially carcinogenic to humans. Long-term acrylamide exposure or intake has been associated with a variety of cancers in mice and rats, including pancreatic, breast, prostate, endometrial, and ovarian cancers. Acrylamide is metabolized to an epoxide metabolite called Glycinamide (GA) in humans and animals by an enzyme called CYP2E1, which causes mutations and DNA disruption. Even though there is ample evidence to support the carcinogenic effects of acrylamide in laboratory animals, there is no relevant evidence that its effects are also carcinogenic in humans according to the few empirical studies conducted so far on dietary and occupational exposure to acrylamide.

The findings indicate that acrylamide can increase the risk of some malignancies. Postmenopausal women exposed to acrylamide are more likely to develop breast and kidney cancers. Several studies have been conducted on acrylamide and its main metabolite, glycidamide, to determine their genotoxicity.

The researchers found that repeated doses of 10 mg/kg of acrylamide for 2 weeks, or single doses of 10, 20, or 30 mg/kg of acrylamide, significantly increased DNA impairment in mice bone marrow cells, as indicated by micronuclei and chromatic aberration. Even though there is ample evidence to support the carcinogenic effects of acrylamide in laboratory animals, there is no relevant evidence that its effects are also carcinogenic in humans according to the few empirical studies conducted so far on dietary and occupational exposure to acrylamide.

Reproductive toxicity

In human beings, no evidence of reproductive toxicity has been reported; however, when rats were given 0.5 to 10 mg/kg of acrylamide, their development was slowed and their sperm count was reduced when compared to the control group. Furthermore, histopathological lesions have also been observed in the testis of treated rats.

When acrylamide (20 mg/kg) was repeatedly injected into male rats for 20 days, their testosterone and prolactin concentrations decreased in a dose-dependent response. A study conducted on female mice treated with acrylamide found reproductive toxicity, with decreased viability of the granulosa cells, corpora lutea, and production of progesterone in their ovaries. When rats were administered 60 mg/kg/day, the mating index and fertility index showed considerable decreases among studied subjects. Male systemic toxicity was found in this investigation at dosage rates of 15, 30, 45, and 60 mg/kg/day, with bodyweight alterations, occurring during the dosing period. In addition, a substantial association between systemic toxicity and reproductive consequences has also been documented in the available literature.

Immunotoxicity

There is no comprehensive review of the literature on acrylamide-induced immune toxicity. An experiment using rats exposed to acrylamide at 50 mg/kg body weight, daily for ten days, reported a reduction in the weight of their thymus and spleen. The lymph nodes in the mesenteric region significantly decreased in size. Additionally, acrylamide was discovered to be immunotoxic in Balb/c female mice, with pathological variations in the thymus, lymph nodes, and spleen, along with decreased body weights, spleen, and thymus weights and lymphocyte numbers. Furthermore, it inhibits the production of interleukin 6, which regulates the immune system, as well as the proliferation of splenocytes.

Hepatotoxicity

Although acrylamide is metabolized in the liver, there have been few human reports of hepatotoxicity. In various animal studies, dietary acrylamide has been shown to cause oxidative stress in the liver. The administration of a dose of (25 mg/kg) acrylamide given to adult rats for 21 days led to a substantial drop in liver GSH levels as well as a significant reduction in overall antioxidant level. In addition, acrylamide also increases liver enzyme levels in the serum. It also decreases the activity of catalase and superoxide dismutase and increases levels of malondialdehyde.

It has been reported to cause significant pathological alterations in the liver, including hypertrophied kupffer cells, hazy edema or hydropic degeneration of hepatic cells, dilated congested blood vessels, and hepatic sinusoids. Necrotic alterations were also observed. Moreover, round cell infiltration was also found in the portal and interstitial tissues. Acrylamide has been found to change the composition of plasma membranes and increase the permeability of the liver parenchymal membrane, which causes active retention of enzymes in the extracellular environment before they enter the blood.
Cardiotoxicity

Acrylamide-induced cardiac abnormalities have not yet been studied in epidemiological studies. In addition, there are only a few studies that suggest cardiotoxicity. There is no denying that acrylamide (2.8 mM for 6 weeks) has the potential to cause cardiotoxicity. Heart tissue histopathology observed hemorrhaging of myocardial muscle fibers as well as degeneration and striation loss, which indicates cardiotoxicity. In terms of cardiac toxicity, long-term exposure to acrylamide may alter the properties of rat cardiomyocytes, such as cell morphology, cell-cell communication, and contraction patterns.

Researchers have investigated how 0.2, 0.4, and 0.6 mg doses of acrylamide affect the development of heart of a chick embryo. Dose-dependent changes in heart tissue were observed: 0.2 mg caused mild deterioration, 0.4 mg caused degenerative and necrotic changes, and 0.6 mg caused defective myocardium. GSH S-transferase, Superoxide dismutase, GSH peroxidase and catalase activity were all reduced, indicating a reduction in antioxidant defence.

Haematotoxicity

Acrylamide binds to haemoglobin when absorbed and is then transported to various organs via body fluid. It binds to reduced glutathione to form conjugates (GSH). Glycidamide is then formed by metabolizing the complex form by using the cytochrome P450 pathway. The final metabolite is genotoxic, causing haemoglobin and glycidamide DNA adduct formation. Furthermore, acrylamide disrupted haematological parameters, decreased erythrocyte membrane resistance, and prevented Hb synthesis. The haematotoxicity was reported on acrylamide administered via gavage to Swiss albino mice at three different dose levels (10, 15, 25 mg/kg/day). A significant decrease in haemoglobin, TLC, DLC, and total protein levels, as well as a highly significant
increase in SGOT and SGPT activity, was observed when compared to the control group. It also affects porcine granulopoiesis at doses of 0.5 and 5 gm/kg of body weight.

**Nephrotoxicity**

Acrylamide is also absorbed into the circulatory system through skin contact and accumulates in the kidneys. A high level of acrylamide exposure has been associated with a decrease in antioxidant function, detoxification capacity, and cellular impairment of visceral organs. Exposure to acrylamide causes vacuolization, infiltration of inflammatory cells and edema in the periglomerular region in renal tubular cells. Acrylamide has been shown to stimulate the expression of inflammatory cytokines including interleukin-1 beta, tumor necrosis factor-alpha, and malondialdehyde.

Among the health effects of Acrylamide, are a decrease in glutathione (GSH) as well as a decrease in levels of enzymatic oxidant and an increase in renal function markers such as blood urea nitrogen and creatinine, which have also been associated with kidney damage. The administration of acrylamide has also been shown to increase levels of renal proinflammatory cytokines, uric acid, creatinine and serum urea in rats, as well as cause lipid peroxidation and DNA.

**Developmental toxicity**

The efficacy of acrylamide on human development has not been studied. According to some reports, these chemicals may be distributed in fetal tissues during pregnancy. There have been studies that indicate the effects of acrylamide during pregnancy. Because acrylamide and glycidamide are water-soluble, they pass easily through the placenta. When embryos of zebrafish were exposed to different concentrations of acrylamide 10,30,100 and 300 mg/L after 6 hours of fertilization in a medium for 114 hours, it caused developmental toxicity including swim bladder deficiency, body curvature, and scoliosis and retention of yolk. It also affected activities that involve locomotion, as measured by distance and speed traveled while swimming.

The availability of information regarding the developmentally harmful effects of acrylamide in rodents is inadequate due to the associated costs. As a result, zebrafish have become increasingly used to study developmental toxicity.

**Acrylamide and oxidative stress**

Oxidative stress occurs when there is an imbalance in the number of free radicals (or reactive oxygen species, ROS, and antioxidants) in our bodies. Free radicals are molecules with an uneven number of electrons that can react with other molecules in our bodies, causing them to oxidise. A variety of cell types are cytotoxic after exposure to acrylamide, and this is associated with increased levels of 3-nitrotyrosine and ROS and activates NOS and Cox.

Orally administered acrylamide caused an increase in thiobarbituric acid reactive substances in rats. The rats exposed to the superoxide anion showed...
elevated levels of SOD activity in the liver, kidney, testes, and brain in response to the increased rate of superoxide anion throughout the body. When animals are exposed to acrylamide, their GSH levels are frequently reduced. When consumptions include chemicals such as hydrogen peroxide, GSH depletion is seen to be significantly higher.

**Conclusion**

Acrylamide is one of the most prevalent toxins in the human diet. It can be found in relatively high concentrations in asparagine-rich foods that have been cooked at a high temperature. Many international organizations, including WHO and the Food and Drug Administration, currently classified acrylamide as a foodborne toxin. The toxic effects of acrylamide could be concluded as neurotoxicity, carcinogenicity and genotoxicity, reproductive toxicity, immunotoxicity, hepatotoxicity, cardiotoxicity, hematotoxicity, nephrotoxicity, and developmental toxicity. Acrylamide toxicity can be caused by a disruption in the antioxidant system. Furthermore, it is widely utilized in industries and is prevalent in dietary foods, so it is not possible to avoid exposure to it. Antioxidant compounds may help reduce acrylamide synthesis in food during processing. To reduce the formation of acrylamide in foods, it is beneficial to modify the processing methods of dietary foods, particularly in carbohydrate-rich foods including potato fries and chips. Further research is needed on the molecular mechanisms of acrylamide toxicity.

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