The Egyptian Journal of Hospital Medicine (January 2023) Vol. 90 (2), Page 2929-2931

Toxic Effects of Acrylamide on Human Health: A Review Article

Rania A. Radwan*[1], Soheir Ali Mohamed[1], Saher M. Gebril[2], Abeer F. EL_Naeem[3], Maha A. Hilal[1]
Departments of [1]Forensic and Clinical Toxicology, [2]Histology and
[3]Anatomy and Embryology, Faculty of Medicine, Sohag University, Sohag, Egypt
***Corresponding author:** Rania A. Radwan, **Mobile:** (+20) 01005327561, **E-Mail:** rania_ahmaed@med.sohag.edu.eg

ABSTRACT

Background: Acrylamide (ACR) is produced in the chemical industry with high volumes such as water-soluble polymers and synthetic organic chemicals. The presence of acrylamide in food was initially assumed to be a result of exogenous contamination. Alarming levels of ACR were first to be discovered in a variety of cooked foods by a Swedish group. The highest levels have been detected in potatoes [fried potato chips and french fries] and grain-based cooked foods using very high temperatures. ACR has major toxic effects on various body systems through multiple mechanisms. ACR was classified as a probable carcinogen to humans.

Objective: The present work aimed to discuss these possible toxic effects on humans, mechanisms, and safety of exposure.

Methods: We researched for data on [Acrylamide, Neurotoxin, Fried potato chips, and French fries] at PubMed, Google Scholar, and Science Direct. However, only the most recent or extensive study was taken into account between August 1999 and September 2022. References from related works were also evaluated by the writers. There are not enough resources to translate documents into languages other than English, hence those documents have been ignored. It was generally agreed that documents such as unpublished manuscripts, oral presentations, conference abstracts, and dissertations did not qualify as a legitimate scientific studies.

Conclusion: Daily consumption of food processed at high temperature make humans at great risk of chronic ACR toxicity which affects greatly human health. Screening for ACR and its active biomarkers in blood and urine is essential in highly susceptible populations as in occupational exposure.

Keywords: Acrylamide, Neurotoxin, Fried potato chips, French fries.

INTRODUCTION

Acrylamide (CH2=CHCONH2) is a water-soluble compound used to produce different chemical and industrial applications at low cost including cosmetics, food processing, agriculture, and water purification. It is also formed by heating food from carbohydrates and amino acid present in the food such as in fried potato products, bread, and coffee. Because of its high water solubility, ACR is easily released to human water supplies[(1,2,3)]**.** Acrylamide is generated in food via the Maillard reaction between asparagine and reducing sugars by heat[(4)].

Previous studies have shown that acrylamide can have a variety of harmful impacts on living things, including the ability to cause cancer, neurotoxicity, or endocrine disruption [(5)].

I- Mechanism of toxicity of ACR:

Song *et al.* [(6)] treated U2OS cells with ACR for 6 and 24 hours before collecting them for further investigation, providing useful proof of the cytotoxicity produced by ACR. A total of 73 important differential metabolites were discovered, and it was shown that ACR reduced autophagic flow, raised reactive oxygen species (ROS) content, elevated apoptosis rates, and secreted inflammatory factors. By lowering the quantities of glycolytic intermediates, reducing the pace of the tricarboxylic acid (TCA) cycle, and increasing the levels of numerous amino acid metabolites and lipid metabolites, exposure to ACR attenuated glycolysis/gluconeogenesis.

According to **Lin *et al.*** [(7)]**,** there is a substantial correlation between urine levels of the oxidative stress byproduct 8-hydroxydeoxyguanosine (8-OHdG) and the acrylamide metabolite N-acetyl-S-(propionamide)-cysteine (AAMA). Nitric oxide synthase (NOS) signaling was implicated, according to immunohistochemical investigations [(8)].

Haridevamuthu *et al.* [(9)] Acrylamide could have a negative impact on the antioxidant defense mechanism. Another aspect to take into account is the adduct that acrylamide creates in presynaptic neurons, which causes neuroinflammation.

Acrylamide's neurotoxicity is caused by interference with nerve energy metabolism, disruption of ion balance, inhibition of axonal transport by binding to microtubules, interference with neuro conduction (causing visible neurotoxicity), and induction of oxidative stress (free radicals cause interference with acetylcholine esterase activity and disruptions of synaptic vesicle fusion, which results in damage to ultrastructure and functional errors) [(10)].

Acrylamide and/or glycidamide binding to spermatid protamines leads to dominant mortality and impacts sperm morphology, which might be used to explain the mechanisms of reproductive toxicity. Because acrylamide may bind to the motor proteins kinesin and dynein, it can cause distal axonopathy, which leads to paralysis in the back legs. It may also cause anesthesia in the penis, which has implications on mounting, intromission, and sperm motility. ACR-induced reproductive and neurological damage does not appear to be directly related to the mutations that are anticipated to result from glycidamide binding directly to DNA [(11)].

Received: 02/10/2022
Accepted: 05/12/2022

II- Safety of ACR exposure:

Prior estimates of the average daily intake of ACR based on dietary contents in western nations ranged from 0.2 to 1.4 g/kg of body weight for adults and from 3.4 g/kg of body weight for lower age groups [12].

Humans ingesting ACR were investigated for safety by **Tardiff *et al.*** [13] For neurotoxicity (non-genotoxicity) and carcinogenicity, a nonlinear dose-response method was used based on modes of action (MoA) (genotoxicity and epigenetic MoA). The estimated tolerated daily intake (TDI) for neurotoxicity from ACR was 40 g/kg/day, whereas the estimated TDIs for cancer were 2.6 and 16 g/kg/day based on ACR or GA, respectively. According to **Tardiff *et al.*** [13], the average ACR consumption margins of exposure (MoE) were 300 and 500, respectively; for cancer, the MoE was 200 and 1200, according to ACR and GA, respectively. MoEs were a little lower for heavy ACR users.

The World Health Organization and the European Union designated 0.1 and 0.5 g/L as the minimum quality requirement levels in drinking water, respectively, whereas the US Environmental Protection Agency set 1 mg/L at monomer levels as the highest permitted limit of acrylamide in water [14].

III- Toxicity of ACR:

1- Neurotoxicity:

The main effects of acrylamide on the nervous system are peripheral neuropathies, although it also damages cerebellar Purkinje cells and degrades distal axons in both the central nervous system and peripheral nervous system. According to **Parzefall** [1], the deterioration of terminal nerves causes harm to the cerebral cortex, thalamus, and hippocampus in addition to impairing cognitive abilities [1].

Studies on neuroretinal toxicity revealed that although the inner nuclear and photoreceptor layers were preserved, chronic exposure to acrylamide resulted in significantly decreased visual function, ganglion cell degeneration, and a reduction in the amplitude of a and b waves on the electroretinogram. Rats exposed to acrylamide during pregnancy experienced severe structural abnormalities in the outer and inner nuclear layers as well as ganglion cell degeneration in the offspring's retinas [15-17]. Experimental evaluation of Acrylamide's neurodegenerative effects on zebrafish was conducted by **Krishnan and Kang**[16] **and Park *et al.***[17].

2- Endocrine:

At every stage of life, endocrine-disrupting chemicals (EDCs) have the potential to disrupt metabolism, growth, and reproduction. This is particularly true during the pubertal and embryonic stages when gene reprogramming can result in poor tissue/organ development and control even in adulthood [18].

a- Effects on reproductive and developmental toxicity:

Different researchers employing 14C-labeled acrylamide have confirmed these results in other species, with consequences on female development and reproduction [19]. Acrylamide harms a female mouse's reproductive system and lowers the quality of her eggs [20]. In addition to sperm maturation, epididymis, Leydig, and Sertoli cells, acrylamide toxicity has also been reported to impair male offspring affection and germ cell mutagenicity [20-22].

b- Effects on thyroid axis:

Examination of the relationship between urinary levels of the acrylamide metabolite (N-acetyl-S-propionamide cysteine) and serum thyroid hormone measurements in adolescents and young adults revealed that the decrease in thyroxine (T4) was associated with an increase in urinary metabolite levels, particularly in women between the ages of 20 and 30. [23].

c- Diabetes Mellitus (DM) and insulin level:

It was discovered via research on DM and ACR hemoglobin biomarkers that there is evidence to support the significance of the hemoglobin acrylamide adduct (HbACR) and hemoglobin glycemide adduct (HbGA)/HbACR in relation to DM. In adults, acrylamide is linked to lower blood insulin levels [24].

3- Genotoxicity:

Although acrylamide exhibits little DNA reactivity in vitro, metabolic activation led to the discovery of new GA-based DNA adducts. Even in the absence of metabolic activity, GA, the main metabolite of ACR, was mutagenic. ACR is one of the few chemicals that causes changes in germ cells [25].

4- Carcinogenicity:

Regarding the risk of human cancer, occupational exposure to AA seems to be the most important factor. Due to their extremely low statistical power, none of the epidemiological investigations demonstrated substantial contributions of ACR to human carcinogenesis. Male and female mice and rats' tumor rates have been observed to have significantly increased [1, 26].

Nucleophilic areas of biomolecules interact with acrylamide and its metabolite, GA. However, although AA and GA react with proteins, only GA forms DNA adducts under settings that mimic in vivo circumstances [26].

CONCLUSION

Daily consumption of food processed at high temperature make humans at great risk of chronic ACR toxicity which affects greatly human health. Screening for ACR and its active biomarkers in blood

and urine is essential in highly susceptible populations as in occupational exposure.

Supporting and sponsoring financially: Nil.
Competing interests: Nil.

REFERENCES

1. **Parzefall W (2008):** Minireview on the toxicity of dietary acrylamide. Food and Chemical Toxicology, 46:1360–1364.
2. **LoPachin R, Gavin T (2012):** Molecular mechanism of acrylamide neurotoxicity: lessons learned from organic chemistry. Environ. Health Perspect., 120: 1650–1657.
3. **Tepe Y (2016):** Acrylamide in surface and drinking water. Acrylamide in food analysis, content and potential health effects, Gokmen V (eds), 1st edition, Elsevier, pp. 275–293. DOI:10.1016/B978-0-12-802832-2.00014-0
4. **Soares C, Alves R, Beatriz M *et al.* (2015):** Factors affecting acrylamide levels in coffee beverages. In the book: Coffee in Health and Disease Prevention, Pp. 217–224. DOI:10.1016/B978-0-12-409517-5.00024-3
5. **Nunes B, Hedlund K, Oliveira M *et al.* (2018):** Ecotoxicological analysis of acrylamide using a microalga as an indicator organism. Water Environ Res., 90: 442–451.
6. **Song D, Xu C, Holck L *et al.* (2021):** Acrylamide inhibits autophagy, induces apoptosis, and alters cellular metabolic profiles. Ecotoxicology and Environmental Safety, 208:111543. https://doi.org/10.1016/j.ecoenv.2020.111543
7. **Lin C, Lee H, Chen Y *et al.* (2013):** Positive association between urinary levels of 8-hydroxydeoxyguanosine and the acrylamide metabolite N-acetyl-S-(propionamide)-cysteine in adolescents and young adults. Journal of Hazardous Materials, 261:372–377.
8. **Wei Q, Li J, Li X *et al.* (2014):** Reproductive toxicity in acrylamide-treated female mice. Reproductive Toxicology, 46:121–128.
9. **Haridevamuthu B, Manjunathan T, Guru A *et al.* (2022):** Amelioration of acrylamide induced neurotoxicity by benzo[b]thiophene analogs via glutathione redox dynamics in zebrafish larvae. Brain Research, 1788: 147941. https://doi.org/10.1016/j.brainres.2022.147941
10. **Kopanska M, Muchacka R, Czech J *et al.* (2018):** Acrylamide toxicity and cholinergic nervous system. J. Physiol. Pharmacol., 69:847-858.
11. **Tyl R, Friedman M (2003):** Effects of acrylamide on rodent reproductive performance. Reprod Toxicol., 17:1–13.
12. **Dybing E, Farmer P, Andersen M *et al.* (2005):** Human exposure and internal dose assessments of acrylamide in food. Food Chem Toxicol., 43, 365–410.
13. **Tardiff R, Gargas M, Kirman C *et al.* (2010):** Estimation of safe dietary intake levels of acrylamide for humans. Food Chem Toxicol., 48(2):658-67.
14. **Eghan K, Lee S, Kim W (2022):** Cardiotoxicity and neurobehavioral effects induced by acrylamide in Daphnia magna. Ecotoxicology and Environmental Safety, 242:113923. doi: 10.1016/j.ecoenv.2022.113923.
15. **Albalawi A, Hasaballah R, Alhasani A *et al.* (2017):** Protective effect of carnosic acid against acrylamide-induced toxicity in RPE cells. Food and Chemical Toxicology, 108: 543-553.
16. **Krishnan M, Kang S (2019):** Vitexin inhibits acrylamide-induced neuroinflammation and improves behavioral changes in zebrafish larvae. Neurotoxicol Teratol., 74: 106811. doi: 10.1016/j.ntt.2019.106811.
17. **Park J, Samanta P, Lee S *et al.* (2021):** Developmental and neurotoxicity of acrylamide to zebrafish. Int J Mol Sci., 22: 3518. https://doi.org/10.3390/ijms22073518
18. **Matosoa V, Bargi-Souzab P, Ivanskia F *et al.* (2019):** Acrylamide: A review about its toxic effects in the light of Developmental Origin of Health and Disease (DOHaD) concept. Food Chemistry, 283: 422–430.
19. **Dearfield K, Abernathy C, Ottley M *et al.* (1988):** Acrylamide: its metabolism, developmental and reproductive effects, genotoxicity, and carcinogenicity. Mutation Research, 19: 45-77.
20. **Duan X, Wang Q, Chen K *et al.* (2015):** Acrylamide toxic effects on mouse oocyte quality and fertility in vivo. Scientific Reports, 5: 11562. doi: 10.1038/srep11562
21. **Wang H, Huang P, Lie T *et al.* (2010):** Reproductive toxicity of acrylamide-treated male rats. Reproductive Toxicology, 29(2): 225–230.
22. **Katen A, Chambers C, Nixon B *et al.* (2016):** Chronic acrylamide exposure in male mice results in elevated DNA damage in the germline and heritable induction of CYP2E1 in the testes. Biology of Reproduction, 95(4) 81-86.
23. **Lin C, Lin L, Chen Y *et al.* (2015):** Association between measurements of thyroid function and the acrylamide metabolite N-Acetyl-S-(propionamide)-cysteine in adolescents and young adults. Environmental Research, 136: 246–252.
24. **Yin G, Liao S, Gong D *et al.* (2021):** Association of acrylamide and glycidamide hemoglobin adduct levels with diabetes mellitus in the general population. Environmental Pollution, 277:116816. doi: 10.1016/j.envpol.2021.116816.
25. **Gamboa da Costa G, Churchwell M, Hamilton L *et al.* (2003):** DNA adduct formation from acrylamide via conversion to glycidamide in adult and neonatal mice. Chem Res Toxicol., 16: 1328–1337.
26. **Baum M, Fauth E, Fritzen S *et al.* (2005):** Acrylamide and glycidamide: an approach towards risk assessment based on biomarker-guided dosimetry of genotoxic/mutagenic effects in human blood chemistry and safety of acrylamide in food. Adv Exp Med Biol., 561: 77-88.