

# A Systematic Review on Association between Dietary Acrylamide and Cancer Risk

**ABSTRACT:** *Acrylamide is really a whitish unscented solid, water soluble and now many organic solvents, organic chemical substance. It is utilised as a predecessor or replacement for various purposes as water-soluble thickeners. It is very poisonous and can thus be oncogenic and is treated as a watery solution. Besides exposure to the industry as well as tobacco, foodstuff seems to be the leading source of human exposure. Cancer continues to have been the second-largest cause of mortality, with a worldwide spike in the volume of cases. Cancer prevention strategies are important for increasing cancer burden. A new meta-analysis about the use of acrylamide related incidence of disease in different locations has been carried out by the experts in view of the current results of wide future studies. 32 publications were discovered either by authors. In order to evaluate the overall likelihood for each cancer site for greatest vs lowest consumption levels including an augmentation in nutritional acrylamide by 10 mg/day, the investigators did a meta-analysis using corrected or spontaneous modelling, based on the heterogeneous approach. Acrylamide has been included as little more than a humans category 2A carcinogen by the International Agency for Research on Cancer backed up by evidence of acrylamide carcinogenicity throughout animals.*

**KEYWORDS:** *Asparagine, Breast cancer, Dietary Acrylamide, Flocculation agents, Maillard reaction.*

## INTRODUCTION

Acrylamide is an industrial chemical that has pure, odourless as well as crystalline structures. It has been available on the market since the mid-1950s and is used largely as a flocculating agent for the purification of drinking water and wastewater though as a settling agent in buildings in the production of electricity and plastics. In 1994, Acrylamide was recognised as potential human carcinogens (2A) by the International Agency for Research on Cancer (IARC), obtained from animal research. Over the last several years, following the publication of our first systematic review and meta-analysis on acrylamide and human cancer, epidemiological data on the relationship between dietary acrylamide and the incidence of many cancers has continued to accumulate [1]. Many findings from large longitudinal studies have recently been published including, among others, the European Prospective Investigation on Cancer and Nutrition (EPIC) and the Nurses' Health Survey (NHS). In particular, the EPIC study published findings for oesophageal, pancreatic, and endometrial cancer, which included over 500,000 participants.

Acrylamide was first reported in products by the Swedish National Food Administration in 2002. The acrylamide is the by-product of the roasting process that develops through the Chemical reaction towards the amino acid asparagine, this same response that caused browning of the food during baking, frying and roasting, by reducing sugar (glucose or fructose) [2]. The levels of acrylamide in cooked meals are therefore determined by parameters including cooking temperatures, heating duration, moisture content as well as the reduction of sugar as well as aspartic acid in the raw foods. Potatoes may have an impact on the diversity of cultivars, the use of fertilisers as well as storage conditions. The storage of potato at 2°C, for particular, leads in an increased concentration of free glucose which transforms potatoes held at the heater to greater levels of acrylamide comparison to 20°C. Acrylamide content variations in many meals and in many of the same foods presented a problem in determining actual intake using widely-used methodologies, including the questionnaire survey (FFQ). These differences frequently present a great problem for those with little or substantial acrylamide consumption, in particular [3].

The finding that acrylamide is generated in human consumption at high temperatures when cooking and is found in typical, high temperature human cooked meals has sparked an interest in the potential carcinogenicity of acrylamide exposure in diet. Acrylamide is produced by the Maillard reaction during food heating between the amino acid asparagine as well as the extraction of sugars, also including sucrose. Throughout recent times, new epidemiological studies were produced, maximum contribution for food exposure to acrylamide were documented as well as labour investigations vulnerable with acrylamide have been amended, but no systematic reviews or meta-analyses were collected. The definitions of exposure were employed in studies linked to diet acrylamide: (i) food acrylamide intake as well as converting chart; (ii) food consuming of slightly elevated boiled potatoes, in particularly acrylamide; and (iii) biomarkers including such protein adducts. Just like with other experimental carcinogens, the assessment of human risk is complicated by issues in the generalization of animal's present measurements to people as well as in the understanding of finds through epidemiologic studies.

A number of epidemiological studies research assessed their probable relationship with cancers in many organisms, including such reproduction bodies, gastrointestinal system, kidney, lung as well as brain since before the identification of acrylate in daily foodstuffs. The consumption of acrylamide has been evaluated using FFQ in most epidemiological investigations whereas some have investigated biomarkers. The quantity of acrylamide in foods, the portion size ingested as well as the frequency of intake as well as the cooking or storage techniques, influence on nutritional acrylamide exposures. Therefore, the variances in world dietary patterns make a major contribution to various food products to acrylamide's dietary consumption. Although the most prevalent suppliers in each country are coffee, fried/baked potatoes as well as bakery products. A thorough overview of the gbe content in foodstuffs or in the overall diet is available in the United State Food and Drug Administration (FDA) database. While in laboratory animals' acrylamide has been proven to be carcinogenic, neurotoxic, as well as unfavourable, inadequate as well as contradictive data is available for its impacts on human health.

Laboratory investigations have shown detrimental effects on both the peripherals as well as the central nervous system, mainly by inhalation of high acrylamide dosage ranging from around 80-1000  $\mu\text{g}/\text{day}$ , corresponding to 1.4-18  $\mu\text{g}/\text{kg}$  body weight/day during acute exposure. Acrylamide and glycidamide, their metabolite of epoxy, are genotoxic and might even act as just an endocrine disruptive agent, affecting the endogenous endocrine system at a smaller concentration compared to environmental research. In instance, acrylamide consumption in pre- as well as premenopausal women is related with changing the reproductive hormones level, namely increasing estradiol as well as follicular stimulation[4]. Previous investigations have been conducted for hormone-dependent gynaecological neoplasia. Many epidemiological findings on acrylamide as well as breast as well as gynaecological cancer have been published, however there have been few systemic investigations on this issue. These findings suggest that the risk of endometrial and ovarian cancers, particularly in people who are not smoking, is minimal but that there is zero breast cancer hazard. No dose-response meta-analysis was performed before. The investigators carried out a meta-analysis of dose - response curve focusing on epidemiological studies on food consumption related chances of breast, endometrial as well as ovaries cancer in people. acrylamide [5].

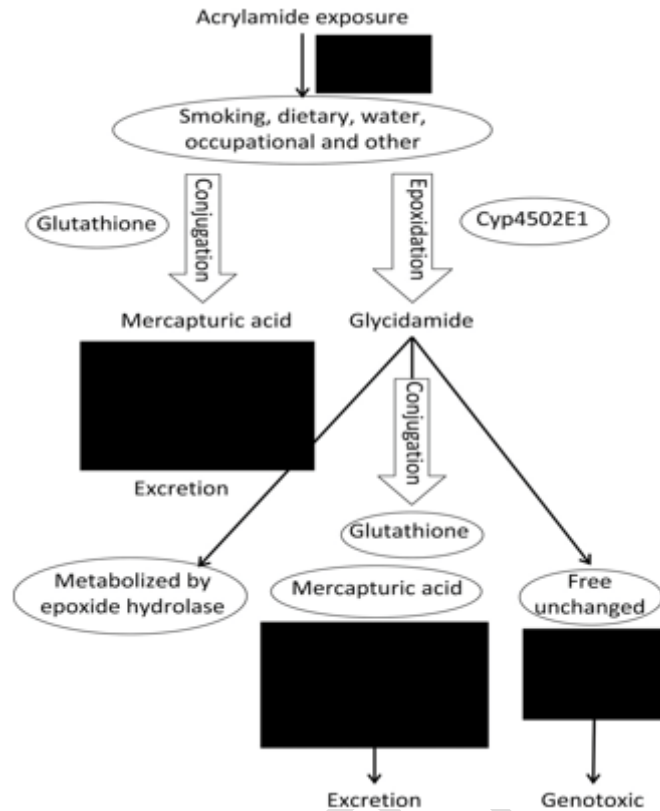
In both females and males' versions, butadiene is cytotoxic to various organs. Acrylamide Carcinogenicity in a range of neurological models, including rats as well as mouse, has been very well established yet, based upon the weights to which human beings are exposed via

food sources, the dosages with in research are 1.000–100.000 times higher than normal levels[6]. Moreover, investigations however have replied that the decomposition of acrylamide differs as well as its metabolites glycidamide have such a four or more times lower inner exposure in people. study about one of the researchers has recently compared epidemiological and laboratory work, and another researcher has conducted 19 nutritional meta-analysis and 6 acrylamide and cancer occupational studies. Alleged infringer as well as three clinical case-control unique investigations, which have been published to present, evaluated the relationship of dietary acrylamide and various kinds of cancer, comprising 11 progressives, 10 cases-cohort, six inhabitants particular instance and 3 hospital-based interior dosages data. Major science publication warehouses, including the PubMed, google as well as the Joint Institute for Food Protection as well as Applied Nutrition (JIFSAN), the World Health Organization (WHO and the FDA), were examined for epidemiology ethanolamine reporting. The literature search focused on documents produced from 2002 to March 2013. The following evaluation phrases have been integrated: dietary production of acrylamide, sources of carboxylate food, consumption to acrylamide, chemicals that are thermally generated, culinary temperatures, the metabolisation of acrylamide as well as hemoglobin intermediates.

### **ACRYLAMIDIC EXPOSURES AS WELL AS INTERNALLY DOSAGE**

Vulnerability to carboxylate to an adult means cumulative ingestion of food, tobacco, second-hand smoke, drinkable water, employment sources, domestic toiletries and goods. The absorption of Acrylamide through dermal penetration is significantly lower, as the skin has a barrier to the absorption of Acrylamide. However, oral usage is crucial in determining the circulation of acrylamide as well as its metabolites inside the body[7]. Acrylamide, which has reported half-lives of 3.1–3.5 hours, is absorbed as well as eliminated in the urine quickly following oral consumption in people. Glutathione conjugation pathways represent an essential role in protecting the body remove acrylamide as urinary metabolites (Figure 1). Acrylamide is sometimes used to epoxidize this same genotoxic intermediate glycidamide via cytochrome P450 2E1 (CYP2E1). Variability in exposure to glycidamide can arise as polymorphisms in CYP2E1 that cause the enzyme to have variable catalytic levels[8]. Furthermore, substances including such allyl as well as di allyl sulphides, that are able to inhibit activities of CYP2E1, can reduce glycidamide production in adults. Bipolar garlic disulfide inhibits CYP2A1 as well as eliminates acrylamide transformation to glycidamide in rats liver[9].has been found to be used. Moreover, the acrylamide bioconversion to glycidamide was down 95 per cent relative to the wild, compared to CYP2E1 nodulous mouse.

In red blood cells, Acrylamide, Glycidamide and now the resultant actin filaments are associated with haemoglobin and give an approximation of something like the internal dosage in which both absorbs and contribute to their metabolism throughout red blood cells' lives (120 days). On instance, smokers have 3 to 5 times haemoglobin adduced acrylamide as well as glycidamide. Second-hand smoke exposure also affects levels of HbAA and HbGA [10].



**Figure 1: The Metabolism of Acrylamide**

## MATERIALS AND METHOD

The actively searching the PubMed/Medline databases systematically until February 25, 2020 using Acrylamide input terms. After evaluating the research results, the analyses were reduced to studies with case-control or cohort designs on exposure to acrylamide in diets and studies providing estimates of risk for breast, endometrial, or ovarian cancer, together with 95 % of confidence intervals (CI) ( $\mu\text{g}/\text{day}$ ). They exclude non-epidemiological research, which do not reveal adjusted hazard calculations, and therefore have conducted acrylamide exposures experiments with haemoglobin intermediates.

### 1. Data Extraction:

For every study, the investigator has gathered Country, quantity, cohort name as well as demographic data, including that of the variety of treatment years, the duration of follow-up; the total as well as necessarily imply age of the respondents. Acrylamide rates were gathered by investigators in the category accessible (e.g. quantiles) and effect size estimations. It also differentiated the complex information on prevalence rates, menopause state, BMI as well as hormone-receptor (breast cancer only) status because once presented whenever produced.

### 2. Data Analysis:

Right off the bat, researchers have meta-analysed the total association measurement (RR-RR, potential danger proportion HR, or odds-RR, as hereinafter described as RR) whilst also going to compare the largest increase to the least inhalation exposure in a multiple regression analysis, with commensurate 95 % of confidence interims (CIs) from each type of cancer. In this work, the scientists assessed the heterogeneity through statistics as well as stratification analysis. The investigators also did a contextual of something like the dose-response, using a current one-stage approach that we previously employed, which permits RRs to be estimated

across a wide range of acrylamide intakes together with their 95% CI. Researchers extracted the mean or median for the exposure categories listed in each sample, depending on which one was available. If unavailable, a value of 20% in front or behind the nearest slashed being input by each classification throughout the simulation, or whether the extreme limits for the highest as well as lower exposure category weren't really recorded. The researcher conducted a generalised minus-square estimation technique in this investigation utilising tiny cubic surfaces utilizing 3 knots at predetermined percentiles (10, 50 and 1990).

To this purpose, researchers take the relationship under accounting with each set of documented RRs as well as combine the structured questionnaire estimates utilising the restricted maximum likelihood approach with multivariable random-effect meta-analysis. Including all studies, the researchers have generally adapted as well as recorded the pitch alongside the form of something like the nonlinear connection created by that of the spline analysis. The researchers showed a visual overlaying of something like the anticipated studies with fixed effect and random in susceptibility assessments. In subsequent studies, a visual overlay was given to demonstrate the influence of the variation across the experiments, including fixed and random effect. All analyses are also re-run by deleting one study at a time to measure the precise impact of the missing analysis on the tests and to assess the heterogeneity as well as source. All quantitative analyses were performed through using 'meta' as well as 'drmeta' routines in the STATA program.

## RESULTS

Total google searches from the database have been verified. Researchers gathered 343 different, title-based as well as abstract screening online articles in the databases, reducing to 22. They deleted four investigations (2 studies, all with qualitative publications), a literary survey as well as a remark, leaving 18 qualitative scientific papers. The cohorts (–11 studies) as well as particular instance (five studies), preceded by two approaches, were by far the most prevalent outlines the proposed. The studies have been published between 2005 as well as 2019, with a large majority in Europe (N=15) following by us And (N=2) and Japan (N=1). Over one kind of cancer has been assessed in certain research. In a total, 10 studies studied breast cancer, 7 endometrial cancers as well as 7 ovarian cancers, totalling 18,100, 3561 and 3,569 breast, endometrial as well as ovarian cancers. Five studies have finally published height and weight stratification results (i.e. <25 and <25 kg/m<sup>2</sup>) and six studies of metastatic breast cancer stratified hormone levels, i.e., androgen receptor level ER and/or progesterin transmitter level PR results. Five papers were available on the same study population and that only the latest and full publications have been included in the analysis in all of these situations.

Researchers did not find evidence of effectiveness throughout cancer risks at higher levels of acrylamide exposition in meta-analysis, summarising RR for breast cancer, 1.03 for endometrial cancer, 1.01 for hepatocellular carcinoma, as well as in significant concentrations of acrylamide exposed in the highest incidence group when compared lowest. Both summary figures were incorrect scientifically. The scientists concluded equivalent results for breast cancer, albeit theoretically ambiguous, limited the research to 0 smokers, but increased chances for endometrial and ovarian cancer. In analysis stratified by menopause, the researchers observed no significant relationship between the factors of exposure to something and breast cancer in pre-menopausal women, as well as an opposite link in postmenopausal individuals. With regards to endometrial cancer, the risk of premenopausal women was lower as well as the danger of longer accessibility was less accurate amongst post menopausal females. The association of thyroid cancer amongst premenopausal women with exposed to acrylamide has been favourable, and yet these results were based solely on 2 studies

indicating opposites while the risks of postmenopausal females have been raised. There have only been results accessible for non-smoking premenopausal women for one research that showed a positive association amongst acrylamide exposure and breast cancer risk. By comparison, there has been no relationship amongst acrylamide consumption, endometrial as well as ovarian malignancies among postmenopausal women as well as favourable connections with breast cancer.

## **DISCUSSION**

This comprehensive systematic analysis of the evidence available on food acrylamide as well as incidence of cancer continues to support earlier indications that more and more cancer sites are not associated, as well as possible small increases in kidney cancer risk but also endometrial as well as ovarian cancer in women who have never start smoking with such a high level of acrylamide. The outcomes of several research were not usually heterogeneous and the test results were verified when just cohort investigations were carried out. In this updated meta-analysis, the number of cases of cancer included has almost quadrupled by including the latest data, mostly from large future cohort studies, published in the last five years. The researchers have thus been able to examine a greater number of cancer locations and acquire an enhanced statistical ability – with some numbers. This notwithstanding, the number of studies is still small for certain cancer sites.

With relation to kidney cancer, the researchers discovered a 20 percent increase in the risk in individuals with low consumption compared to the low acrylamide in diet using data from three studies as well as longitudinal direction investigations. Approximately 50 percent of the gains were slightly greater given simply the latter research size. On either side, there really was no meaningful association because when analysis was conducted with continuous exposure measurements (+2% at risk with such an increase in dietary acrylamide of 10 µg/day). The aforementioned results were nonetheless impacted, in Swedish case-check investigations, by the corresponding variability across sample estimates, ranging 0.91 to 1.10 throughout the NCS. Different analyses of design results could at least partly justify this and prospective design likewise reveal considerably greater risk levels. Smoking is also a potential cause as well as a significant source of exposed to acrylamide for kidney cancer. Consequently, the connection between dietary acrylamide as well as bladder cancer may be unclear or changing. There have also been specific evidence indicating the function that acrylamide exposures to renal cancer could play in two occupational cohort studies. Consequently, the subject is still up to dispute, despite the little but borderline relationship and the already little epidemiology information of bladder cancer.

## **CONCLUSION**

In the evaluated observational studies that contributed to potential misinterpretation, the nutritional acrylamide hazard identification was inadequate. Both in case and control groups, case control studies also revealed approximately the same amount of exposures to nutritional acrylamide. For illness objectives including such cancers, vulnerability evaluation approaches present in numerous exposures are strongly recommended. However, the majority of the epidemiological studies evaluated have approximated one-off baseline FFQ doses with such a strong assumption that both dietary acrylamide as well as person exposures were consistent over time. This is particularly important it seems like every year, a number of new foodstuffs are put on the market. Moreover, rhythms of calorie consumption may be changed, resulting in possible dietary alterations to acrylamides, including seasonality, prices, marketing and social factors including such holidays, etc.

## **REFERENCES**

- [1] M. K. Virk-Baker, T. R. Nagy, S. Barnes, and J. Groopman, "Dietary acrylamide and human cancer: A systematic review of literature," *Nutrition and Cancer*. 2014.
- [2] C. Pelucchi, C. Bosetti, C. Galeone, and C. La Vecchia, "Dietary acrylamide and cancer risk: An updated meta-analysis," *Int. J. Cancer*, 2015.
- [3] B. P. Riboldi, Á. M. Vinhas, and J. D. Moreira, "Risks of dietary acrylamide exposure: A systematic review," *Food Chemistry*. 2014.
- [4] N. Mourouti, M. D. Kontogianni, C. Papavagelis, and D. B. Panagiotakos, "Diet and breast cancer: A systematic review," *Int. J. Food Sci. Nutr.*, 2015.
- [5] R. C. R. Albuquerque, V. T. Baltar, and D. M. L. Marchioni, "Breast cancer and dietary patterns: A systematic review," *Nutr. Rev.*, 2014.
- [6] A. Dandamudi, J. Tommie, L. Nommsen-Rivers, and S. Couch, "Dietary patterns and breast cancer risk: A systematic review," *Anticancer Research*. 2018.
- [7] T. Kocadağlı and V. Gökmen, "Metabolism of Acrylamide in Humans and Biomarkers of Exposure to Acrylamide," in *Acrylamide in Food: Analysis, Content and Potential Health Effects*, 2016.
- [8] L. Pellé *et al.*, "Association between CYP2E1 polymorphisms and risk of differentiated thyroid carcinoma," *Arch. Toxicol.*, 2016.
- [9] Y. F. Huang *et al.*, "The modifying effect of CYP2E1, GST, and mEH genotypes on the formation of hemoglobin adducts of acrylamide and glycidamide in workers exposed to acrylamide," *Toxicol. Lett.*, 2012.
- [10] M. Obón-Santacana *et al.*, "Dietary and lifestyle determinants of acrylamide and glycidamide hemoglobin adducts in non-smoking postmenopausal women from the EPIC cohort," *Eur. J. Nutr.*, 2017.