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College of Veterinary Medicine

Study the Side Effect of acrelamide in body systems

A Graduation Project Submitted to the Department Council of the Internal and Preventive Medicine-College of Veterinary Medicine/ University of Al-Qadisiyah in a partial fulfillment of the requirements for the Degree of Bachelor of Science in Veterinary Medicine and Surgery.

By

Yasser Hassan Hasseb

Supervised by

Assist Prof.Dr. Saadeya Ali Al_Gnami

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بِسۡمِ ٱللَّهِ ٱلرَّحۡمَٰنِ ٱلرَّحِيمِ

فَتَعَٰلَى ٱللَّهُ ٱلۡمَلِكُ ٱلۡحَقُّۗ وَلَا تَعۡجَلۡ بِٱلۡقُرۡءَانِ مِن قَبۡلِ أَن يُقۡضَىٰٓ
إِلَيۡكَ وَحۡيُهُۥۖ وَقُل رَّبِّ زِدۡنِي عِلۡمٗا ١١٤

صَدَقَ ٱللَّهُ ٱلۡعَظِيمُ

من سورة طه

Certificate of Supervisor

I certify that the project entitled (**Study the Side Effect of acrelamide in body systems**

was prepared by **Yasser Hassan Haseeb** under my supervision at the College of Veterinary Medicine / University of Al-Qadisiyah.

Supervisor

Assist Prof.Dr. Saadeya Ali Al_Gnami

Dept. of Physiology and Pharmacy

Coll. Of Vet.Med./ Univ. of Al-Qadisiyah.

-- / -- / 2021

Certificate of Department

We certify that **Yasser Hassan Haseeb** has finished his/her Graduation Project entitled (**Study the Side Effect of acrelamide in body systems**) and candidate it for debating.

Instructor

Assist. Prof . Dr. Saadeya Ali Al_Gnami

-- / -- / 2021

Head of Dept of Int. and Prev. Med.

Assist. Prof. Dr. Saad Hashim Al-Husseiny

-- / -- / 2021

Dedication

To my Lovely friend ... My father

To my supporter ... My Mother

Acknowledgements

First and foremost, praises and thanks to the God, the Almighty, for His blessings throughout my research work to complete the research successfully.

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Abstract

Acrylamide (AA) is a highly reactive organic compound capable of polymerization to form polyacrylamide , which is commonly used throughout a variety of industries . Given its toxic effect on humans and animals , the last 20 years have seen an increased interest in research devoted to the AA. One of the main sources of AA is food . AA appears in heated food following the reaction between amino acids and reduced sugars . Large concentrations of AA can be found in popular staples such as coffee , bread or potato products. An average daily consumption of AA is between 0.3-2.0 μg/kg b.w. Inhalation of acrylamide is related with occupational exposure .

AA delivered with food is metabolized in the liver by cytochrome P450 . AA biotransformation and elimination result in formation of toxic glycidamide (GA) . Both, AA and GA can be involved in the coupling reaction with the reduced glutathione (GSH) forming glutathione conjugates which are excreted with urine . Biotransformation of AA leads to the isturbance in the redox balance .

Chapter one
Introduction

Acrylamide is a chemical that can form in some foods during high-temperature cooking processes , such as frying, roasting, and baking . Acrylamide in food forms from sugars and an amino acid that are naturally present in food ; it does not come from food packaging or the environment . (Prineas J., 1969: 614)

Acrylamide is an organic compound that is formed specifically when certain foods are prepared at low moisture and at temperatures usually above 120 °C, such as in the case of baked, roasted or fried foods including French fries, potato crisps , breads , biscuits and coffee beans . It results from a reaction between sugars and certain amino acids (the constituents of proteins) such as asparagine . This is called the ‘Maillard reaction’, it is what gives browned food a distinctive color and taste . Acrylamide is also formed and present in cigarette smoke .(KUPERMAN AS, 1958: 180)

Chapter Two

Review of Literature

General effects that acrylamide can produce

In both laboratory animals and humans, acrylamide passes through the gastro intestinal tract and reaches the bloodstream . It can cross the placenta and is transferred to a small extent into human milk . (Prineas J., 1969: 615)

To facilitate its excretion the body transforms acrylamide into other molecules, one of them being glycidamide , which is considered to be the molecule that causes the genotoxicity and carcinogenicity of acrylamide .

Glycidamide can bind itself to DNA or to proteins such as haemoglobin . Acrylamide and glycidamide can be further broken down into mercapturic acids that are excreted into urine and the analysis of their presence can be used as a marker to determine exposure to acrylamide . (KUPERMAN AS, 1958: 183)

In laboratory animals, exposure to acrylamide at high enough doses can have a variety of effects , but the main effects are toxicity to the nervous system , mutations and damage to chromosomes , and carcinogenicity . (Garland TO, 1967: 137)

In humans , studies of people who are exposed to acrylamide through their work did not indicate an increased cancer risk . There is also no consistent indication from available studies for an association between acrylamide exposure through food and an increased risk of most cancers . A few studies suggested an increased risk for renal , endometrial and ovarian cancer but the evidence is limited and inconsistent .

Two studies reported an inverse relationship between acrylamide exposure and weight at birth and other markers of fetal growth but it has not been established whether or not this association is causal .

Studies among workers occupationally exposed to acrylamide showed an increased risk of neurological alterations , including mostly the peripheral but also the central nervous system . However in most cases these symptoms were reversible .

Is there a risk of adverse effects from acrylamide from food or other types of exposure ?

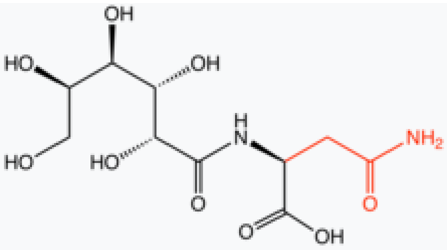
By comparing the estimated exposure calculated from diet with the highest levels of exposure at which no health effects were observed , a margin of exposure (MOE) can be calculated . In this case , the margins of exposure ranged from 50 to 425 depending on the population groups . Since the EFSA Scientific Committee considers that for substances that are both carcinogenic and genotoxic , a margin of exposure of 10 000 or higher would be the level of low concern from a public health point of view, a concern remains with respect to the risk of cancer, even if there is no clear experimental or epidemiological (human) evidence that acrylamide causes cancer in humans.

The CONTAM Panel also noted that acrylamide is a mutagen for germ cells and that there are at present no established procedures for risk assessment using this endpoint. Finally the Panel made a series of recommendations to improve the risk assessment related to the exposure to acrylamide in the future. (Garland TO, 1967: 138)

Chemical characteristics

Acrylamide can be prepared by the hydrolysis of acrylonitrile. The reaction is catalyzed by sulfuric acid as well as various metal salts. It is also catalyzed by the enzyme nitrile hydratase. US demand for acrylamide was 253,000,000 pounds. (115,000,000 kg) as of 2007, increased from 245,000,000 pounds (111,000,000 kg) in 2006.

Acrylamide arises in some cooked foods via a series of steps initiated by the condensation of the amino acid asparagine and glucose. This condensation, one of the Maillard reactions followed by dehydrogenation produces *N*-(D-glucos-1-yl)-L-asparagine, which upon pyrolysis generates some acrylamide. (KUPERMAN AS, 1958: 190)



N-(D-glucos-1-yl)-L-asparagine, precursor to acrylamide in cooked food .

The Acrylamide effects on the body system :

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. Results 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 . An inverse relation between acrylamide exposure and birth weight and other markers of fetal growth is reported in two studies . EFSA's experts concluded that more research is needed to confirm these results from human studies . Studies on workers exposed to acrylamide in the workplace show an increased risk of disorders to the nervous system . (Garland TO, 1967: 138)

The effects of Acrylamide on nervous system

The neurologic effects of acrylamide on the cat have been described and some of the neural loci of the intoxication elucidated. The nature of the syndrome depended upon the dose magnitude, rate of administration and the length of time during which the agent was given . Severe tonic-clonic convulsions and other signs of a diffuse central excitation were produced by lethal doses . The repeated or single administration of sub lethal doses gave rise to a chronic and reversible intoxication. This was characterized by an ataxia and tremor which were identical to those of cerebellar a synergia . No other biological effects were apparent at the dose levels required to initiate this syndrome. Histological alterations in neural tissue have not been revealed . (Prineas J., 1969: 620)

Scientists have known for years that acrylamide is capable of causing nerve damage in humans, including muscle weakness and impaired muscle coordination, particularly from industrial exposure to large levels of the chemical . new laboratory studies suggest that chronic dietary exposure to the chemical is capable of damaging nerve cells in the brain and could potentially play a role in the development of neurodegenerative disease, including Alzheimer's , according to Richard LoPachin, Jr., Ph.D., a neurotoxicologist with Albert Einstein College of Medicine in New York . He notes that acrylamide is structurally similar to acrolein, a chemical found in increased levels in brains of patients with Alzheimer's and other neurodegenerative diseases .

Dietary acrylamide may play a role in Alzheimer's

Scientists have known for years that acrylamide is capable of causing nerve damage in humans , including muscle weakness and impaired muscle coordination , particularly from industrial exposure to large levels of the chemical. Now, new laboratory studies suggest that chronic dietary exposure to the chemical is capable of damaging nerve cells in the brain and could potentially play a role in the development of neurodegenerative disease , including Alzheimer's, according to Richard LoPachin , Jr., Ph.D., a neurotoxicologist with Albert Einstein College of Medicine in New York . He notes that acrylamide is structurally similar to acrolein, a chemical found in increased levels in brains of patients with Alzheimer's and other neurodegenerative diseases . Studies in humans are warranted, the researcher says .

How was dietary exposure evaluated ?

In order to evaluate the exposition of the population to acrylamide through food, a large number of measurements of acrylamide in food was compiled and combined with survey data on the diet consumed across Europe . The highest concentrations were found in coffee and potato crisps . Estimation of human exposure to acrylamide revealed that infants, toddlers and other children were the most exposed population groups , with the highest exposures at 3.4 µg/kg b.w. per day , whereas the highest exposures in other groups were at 2.0 µg/kg b.w. per day . Scenarios were designed in order to assess the influence of specific behaviours (e.g. preference for particular products, places of consumption , home-cooking habits) on the total dietary exposure to acrylamide, and the highest variation came from conditions of potato frying from which the total dietary exposure to acrylamide could be increased up to 80 % . (Garland TO, 1967: 146)

Acrylamide in food

Acrylamide ($CH2=CH–CO–NH2$, according to IUPAC : 2-propenamid) is a highly reactive , organic, white and crystal substance, with molecular weight of 71.08 g (Żyżelewicz et al. 2010). AA is a polar substance which easily dissolves in water or other polar solvents, e.g. in methanol or ethanol (Jankowska et al. 2009).

High reactivity of AA is connected with the double bond and amide group . The compound may create hydrogen bonds and can react both with amide and vinyl groups (Girma et al. 2005, Żyżelewicz et al. 2010).

Acrylamide is polymerized under the influence of temperature and UV radiation. These reactions result in creation of new chemical compounds called polyacrylamides Recent years revealed a considerable increase in investigation of acrylamide as a potentially dangerous substance to people . In early 2000s, Swedish researchers proved that certain foods might contain large concentrations of acrylamide (Lofstedt 2003).

The research by Tareke et al. (2002) indicated that food processing has influence on acrylamide formation . The factors influencing the occurrence of AA in the food are: temperature, exposure time to high temperature, the amino acids content and their types and the content of carbohydrates in the food (Becalski et al. 2003, Konings et al. 2003).

AA is formed during frying, deep frying and baking foods rich in carbohydrates and especially in amino acid – asparagine . High concentrations of AA are found in processed foods like: chips (50-3500 µg/kg), frites (170-2287 µg/kg), coffee (170-350 µg/kg), bread (70-430 µg/kg) or corn flakes (30-1400 µg/kg) (Friedman 2003).

Acrylamide concentrations in selected foodstuffs together with methods of measurements of acrylamide concentration in food are presented The mechanism of AA formation in food has not been clearly described yet . Numerous research has shown only hypothetical ways in which AA is being formed in comestible products (Edegaard et al. 2008, Mestdagh et al. 2008).

Most of the research point to asparagine presence as a significant factor contributing to AA formation (Zhang et al. 2009, Taeymans et al. 2004).

The reaction between glucose (reducing sugar) and asparagine gives a product responsible for the food's flavor and color . This reaction is known as a Millard's reaction and it has a higher rate at the temperature exceeding 120 °C (Friedman 2003, Tareke et al. 2002).

The content of AA increases considerably during frying, grilling and roasting. Popular foodstuffs such as coffee, high-in-starch potato products and cereal products contain large amounts of AA (Claus et al. 2008, TajnerCzopek et al. 2012).

People are also exposed to harmful effects of AA by consuming natural unprocessed products rich in asparagines, including asparagus, cocoa beans or cereals (Rachwał and Nebesny 2012). According to the European Food Safety Authority (EFSA) report, the level of AA in food ranges from under 30 µg/kg to 4700 µg/kg, depending on the product (EFSA 2009, Mojska and Gielecińska 2012).

Research also shows that exposure to AA varies and depends mainly on the population, age of consumers and their eating preferences. In European populations, mean daily intake of acrylamide goes from 0.14 to 1.31 µg/kg body weight. Similar mean intake (0.43-1.1 µg/kg body weight per day) was indicated in the United States (Dybing and Sanner 2003).

The research conducted in Kraków, Poland by Jankowska et al. (2009) indicated that AA was excessively consumed by children and teenagers. Among children and adults, bread – a product eaten on a daily basis, is the main source of AA. Other Polish research indicated that an average AA consumption in children aged 1-6 years was about 0.47 µg/kg b.w. per day and among children aged 7-18 years it was 0.34 µg/kg b.w. per day . (Mojska and Gielecińska 2012).

Maximum intake of acrylamide reaching 7.9 and 8.1 µg/kg b.w. per day was estimated in 13 years old Norwegian boys and girls respectively (Dybing and Sanner 2003).

Table 1. Acrylamide content in analyzed products.

Author	Number of food samples	Analysis of acrylamide in food	Acrylamide content	Products with the highest acrylamide content	Highest mean acrylamide content (µg/kg)
Claeys *et al.* 2010	1725	LC-MS	34-2814 µg/kg (mean)	Coffee substitute	2814±1045
				Instant coffee	694±81
				Potato crisps	525±477
				Gingerbread	431±455
Sirot *et al.* 2012	192	LC-MS	2-954 µg/kg (range)	Potato chips	954±240
				French fries	724±358
				Cocktail biscuits (salted)	697±430
				Chocolate biscuits	139±100
Konings *et al.* 2003	341	LC-MS-MS	<30-3100 µg/kg (range)	Potato crisps	1249±656
				Cocktail snacks	1060±950
				Gingerbread	890±393
				Chips (deep-fried)	351±297
Mojska and Gielecińska 2012	111	GCQ-MS/MS LC-MS/MS	2-516 µg/kg (range)	Follow-on formula	73±78
				Infant biscuits	219 ±139

LC-MS – liquid chromatography-mass spectrometry, LC-MS-MS – liquid chromatography tandem mass spectrometry, GCQ-MS/MS – gas chromatography with tandem mass spectrometry, LC-MS/MS – liquid chromatography with tandem mass spectrometry.

The Health Effects Of Acrylamide And How Can It Be Reduced In Food .

Some studies have linked high levels of acrylamide to cancer in animals and neurological damage in humans. Despite uncertainties over acrylamide's actual health effects at the levels found in food, there is heightened public awareness about this compound .(Garland TO, 1967: 138)

The potential health effects of acrylamide and ways to reduce its content in foods will be explored Aug . 21-23 in a three-day symposium, Chemistry and Toxicology of Acrylamide , during the 234th national meeting of the American Chemical Society .

The following are brief summaries of selected papers .

Acrylamide found in dried fruits

Dried fruits, which are rich in fiber and antioxidants , have long been promoted as healthful alternatives to fresh fruits. Now, Thomas Amrein and his associates at the Swiss Federal Institute of Technology have found acrylamide in dried fruits, a surprising finding considering that these products are dried at relatively mild temperatures instead of the high temperatures , through baking and frying , that usually produce the chemical . The study suggests that acrylamide is capable of being formed under relatively mild conditions through reactions that are not fully understood , the researchers say . Of the different dried fruits tested, the highest concentrations of the chemical were found in dried pears and prunes . (KUPERMAN AS, 1958: 195)

Fat found to be significant source of acrylamide in food

Studies have shown that carbohydrates and amino acids , particularly the non-essential amino acid asparagine , are the main chemicals in food that are responsible for acrylamide formation . Now, a new study by researchers in Spain indicates for the first time that dietary fats make a significant contribution to the formation of acrylamide . The researchers found that high fat levels in roasted almonds may account for as much as half of the acrylamide found in this food and likely accounts for high levels found in other high fat foods , according to study leader Francisco J. Hidalgo, Ph.D., of the Instituto de la Grasa in Seville . Although the researchers say they have not yet demonstrated that reducing fat content in foods actually reduces acrylamide , the study provides a new target to consider in efforts to reduce acrylamide formation .(Garland TO, 1967: 138)

Farming techniques, biotechnology may help lower acrylamide

Researchers in England are experimenting with novel agricultural practices and biotechnology in an effort to help reduce acrylamide levels in food crops . Nigel Halford, of Rothamsted Research , in collaboration with the University of Reading, says that increasing soil sulfur levels in wheat crops and reducing nitrogen availability in crops can decrease levels of asparagine, an acrylamide precursor . The researchers have also produced a new variety of potato through genetic modification that contains lower sugar levels than conventional potatoes and are targeting plant genes responsible for controlling asparagine levels in an effort to reduce acrylamide levels in food crops . (Garland TO, 1967: 166)

Acrylamide not linked to breast cancer in U.S. women

Foods that contain acrylamide are unlikely to cause breast cancer, according to preliminary results of a new study involving 100,000 U.S. women followed over a 20 year period . The study is the largest epidemiological study to date exploring the possible link between acrylamide and cancer in humans. Led by Lorelei Mucci, ScD, an epidemiologist at Harvard University School of Public Health in Boston, the study found that the incidence of breast cancer among women whose acrylamide consumption was considered high was roughly equal to the incidence among those whose acrylamide consumption was low. For further information. (KUPERMAN AS, 1958: 180)

How to avoided

Some people working in certain industries that are regulated for acrylamide need to take precautions to limit their exposure .

For most people , the major potential sources of acrylamide exposure are in certain foods and in cigarette smoke . Avoiding cigarette smoke can lower your exposure to this and other harmful chemicals . (Bradley WG, Asbury AK, 1970: 500)

It’s not yet clear if the levels of acrylamide in foods raise cancer risk, but if you’re concerned , there are some things you can do to lower your exposure . In general, acrylamide levels rise when cooking is done for longer periods or at higher temperatures and when certain types of cooking methods are used (such as frying or roasting). Here are some ways to reduce exposure to acrylamide in foods, according to the FDA : (Dybing and Sanner 2003 : 116).

- Limit foods that might be high in acrylamide , such as potato products (especially French fries and potato chips), coffee, and foods made from grains (such as breakfast cereals, cookies , and toast).

- Limit certain cooking methods , such as frying and roasting, and limit the time certain foods are cooked . Boiling and steaming do not produce acrylamide .
- Soak raw potato slices in water for 15 to 30 minutes before frying or roasting to reduce acrylamide formation during cooking . (Soaked potatoes should be drained and blotted dry before cooking to prevent splattering or fires)
- If frying potatoes or toasting bread, cook them to a lighter color (as opposed to dark brown), which produces less acrylamide .
- Avoid storing potatoes in the refrigerator, which can result in increased acrylamide levels during cooking . (Garland TO, 1967: 166)

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