ACRYRED

Deliverable 5.2 – DRAFT Strategic Agenda for Acrylamide Research in the Fields of Health Impacts of Maillard Reaction Products (2024-2029)

Project Name	ACRYRED
Delivery Date	10/12/2024
Working Group	WG5
Authors	Zuzana Ciesarova (National Agricultural and Food Centre, Food Research Institute in Bratislava, Slovakia)
Grant Period	GP2

cost
EUROPEAN COOPERATION IN SCIENCE & TECHNOLOGY

Funded by the European Union

Executive Summary

The main objective of the WG5 is to enable a dialogue on the parameters that should be considered in a risk – benefit analysis of Maillard reaction products and the impact of mitigation measures on the risk – benefit balance.

This objective requires an interdisciplinary approach and cooperation between the working groups, especially with WG3. In Grant Period 2, WG5 activities have focused on supporting the above objective under Tasks 5.1, 5.2 and 5.3, namely the establishment of an active platform of WG5 members through virtual and face-to-face meetings, as well as joint meetings with WG5 members, the promotion of project information through conferences and webinars, and the sharing of information through various means (exhibitions, seminars, websites, communication media). Most valuable was to provide expert information, professional experience, and tutorials through the Training School, including lectures and practical sessions on the evaluation of acrylamide mitigation measures in food technology. The Proceedings of this Training School are available to all CA members.

The strategic agenda for acrylamide research, focused on the health effects of Maillard reaction products, was developed through the joint efforts of WG3/WG5 members during their meeting in Zagreb (8–9 April 2024). Despite more than two decades of research, definitive evidence of acrylamide's impact on human health remains lacking, underscoring the need for further toxicological studies. A comprehensive, multidisciplinary approach that integrates toxicology, epidemiology, and risk impact modelling is crucial to better understand potential risks and shape effective regulatory frameworks. This strategy seeks to balance immediate risk mitigation with long-term research priorities, enabling the food industry to address emerging health and regulatory challenges while ensuring consumer trust and product quality. Collaboration among academia, industry, and regulatory bodies will be key to achieving these objectives.

Authors and Reviewers

Main Responsible		
Organization	**Name**	**Mail**
National Agricultural and Food Centre, Food Research Institute in Bratislava, Slovakia	Zuzana Ciesarova	zuzana.ciesarova@nppc.sk
Author(s) / Contributor (s)		
Organization	**Name**	**Mail**
National Agricultural and Food Centre, Food Research Institute in Bratislava, Slovakia	Zuzana Ciesarova	zuzana.ciesarova@nppc.sk
Hacettepe University, Ankara, Turkey	Vural Gökmen	vgokmen@hacettepe.edu.tr
University of Reading, U.K.	Jane K Parker	j.k.parker@reading.ac.uk
University of Minnesota, U.S.A.	Christine Nowakowski	cnowakow@umn.edu

People providing their names in the table above are providing their consent in sharing their information in this document

Legal Disclaimer

This Report is based upon work from COST Action ACRYRED, CA21149, supported by COST (European Cooperation in Science and Technology).

COST (European Cooperation in Science and Technology) is a funding agency for research and innovation networks. Our Actions help connect research initiatives across Europe and enable scientists to grow their ideas by sharing them with their peers. This boosts their research, career and innovation

Views and opinions expressed are however those of the author only and do not necessarily reflect those of the European Union or of the COST Association. Neither the European Union nor the COST Association can be held responsible for them.

Table of Contents

Introduction

ACRYRED COST Action is aimed to "Reducing Acrylamide Exposure of Consumers by a Cereals Supply-chain Approach Targeting Asparagine". ACRYRED's challenge is to establish a multi-disciplinary research and communication network on reducing acrylamide formation, involving the entire value chain from grains to consumer products. ACRYRED brings together plant breeders, the agricultural grain farming community, grain traders, European food processors, toxicologists, public regulators and consumer interest groups to establish research requirements on asparagine formation in plants, as well as investigate new economic models that encompass the full supply chain. The Action will also elaborate new approaches to inform catering/hospitality and consumers about responsible cooking of cereal-based foods. ACRYRED is formed by 5 Working Groups (WG): WG1 "Interdisciplinary Exchange and Integration of Knowledge on Asparagine and Acrylamide"; WG2 "Agronomy and Plant Breeding"; WG3 "Chemistry & Processing"; WG4 "Cereal Supply Chain Economy"; and WG5 "Risk-benefit of MR Products and its Mitigation".

The objective of WG5 "Dialogue on risk-benefit of MR products associated with cereals and impact of mitigation measures" is to enable a dialogue on the parameters that should be considered in a risk – benefit analysis of MR products and impact of mitigation measures on the risk – benefit balance.
The main tasks of WG5 have been defined as follows:

- Task 5.1 To make a detailed overview of the relevant research in risk – benefit balance of MR products as relevant to cereal-based foods.
- Task 5.2 To align amongst stakeholders on a draft a strategic research agenda for the field.
- Task 5.3 To develop content for the ACRYRED training school on the risk – benefit balance of MR products, and to identify candidates for participation in this training school.

Objectives of the document

The objective of this document is to fulfil ACRYRED Deliverable 5.2: to propose a draft strategy for Acrylamide Research in the Fields of Health Impact of Maillard Reaction Products (2024-2029). This deliverable was developed based on round table discussions during the Zagreb joint WG3/WG5 workshop held on the 9th of April 2024 in Zagreb. It will be further developed to produce a final Agenda for the next 5 years for research in the field of health impact of Maillard reaction products (Deliverable 5.3).

1. Chapter 1 - Health Risks Associated with Acrylamide Exposure: Status Quo

Acrylamide is a chemical compound that forms during high-temperature cooking processes such as frying, baking, or roasting, particularly in carbohydrate-rich foods. Its discovery in foods in 2002 raised concerns due to its classification as a probable human carcinogen by the International Agency for Research on Cancer (IARC). This report provides an overview of the health implications of acrylamide in foods, including its formation, potential risks, and recommendations for minimizing exposure.

1.1 Formation of Acrylamide in Foods

Acrylamide forms predominantly through the Maillard reaction, a chemical process that occurs between asparagine (an amino acid) and reducing sugars like glucose or fructose when foods are heated above 120°C (248°F). Foods particularly prone to acrylamide formation include:

- Starchy foods such as potato chips, French fries, and bread.
- Coffee due to roasting.
- Certain baked goods, like cookies and crackers.

Factors influencing acrylamide levels include cooking time, temperature, and the specific composition of the food.

1.2 Health Risks Associated with Acrylamide

Acrylamide has been a topic of scientific investigation due to its potential health risks. The compound's adverse effects are primarily linked to its metabolism into glycidamide, a highly reactive molecule that can interact with DNA and proteins, leading to mutagenic and toxic effects. Below is a detailed discussion of the health risks associated with acrylamide exposure:

1.2.1 Carcinogenic Potential

- **Mechanisms of Action**
  Acrylamide is metabolized in the body by cytochrome P450 enzymes into glycidamide, which can form adducts with DNA. These DNA adducts can lead to mutations, potentially initiating cancer development.

- **Animal Studies**
  Extensive research in rodents has shown that high doses of acrylamide can induce tumors in multiple organs, including the mammary glands, thyroid, lungs, and reproductive organs. These findings underpin its classification as a *probable human carcinogen* by the International Agency for Research on Cancer (IARC).

- **Human Studies**
  Epidemiological evidence on acrylamide's carcinogenicity in humans is inconclusive. Large-scale studies have explored the link between dietary acrylamide intake and cancers such as breast, ovarian, and colorectal cancer, with mixed results. Variability in individual exposure levels, dietary habits, and genetic susceptibility complicates definitive conclusions.

1.2.2 Neurotoxic Effects

- **Occupational Exposure**
  High levels of acrylamide exposure in industrial settings, such as manufacturing and chemical plants, have been associated with neurotoxic symptoms. These include peripheral neuropathy, muscle weakness, and impaired motor function.

- **Dietary Exposure**
  The levels of acrylamide found in food are significantly lower than occupational exposures, but long-term dietary intake could pose subtle neurotoxic risks. However, evidence from human studies is limited and does not show clear neurotoxic effects from dietary acrylamide.

1.2.3 Reproductive and Developmental Toxicity

- **Animal Studies**
  Acrylamide has been shown to cause reproductive toxicity in animal models. Male rodents exposed to high doses of acrylamide exhibited reduced sperm count, motility, and fertility. Female rodents experienced adverse effects on ovulation and fetal development.

- **Human Implications**
  Data on humans is limited, but the potential for acrylamide to disrupt reproductive health is a concern. Pregnant women may need to minimize exposure to reduce potential risks to fetal development.

1.2.4 Genotoxicity and Mutagenicity

- Glycidamide, a metabolite of acrylamide, can directly interact with DNA, leading to the formation of DNA adducts. These adducts can cause genetic mutations, which are critical steps in carcinogenesis.

- Acrylamide has demonstrated mutagenic effects in laboratory studies, although the relevance of these findings to low-level dietary exposure in humans is still being explored.

1.2.5 Other Chronic Health Risks

- **Oxidative Stress**
  Acrylamide has been linked to increased production of reactive oxygen species (ROS) in cells. Oxidative stress can contribute to chronic conditions, including cardiovascular diseases, diabetes, and neurodegenerative disorders.

- **Inflammation**
  Acrylamide and its metabolites may trigger inflammatory responses, which can exacerbate the development of diseases like atherosclerosis and metabolic syndrome.

1.2.6 Vulnerable Populations

Certain groups may be more susceptible to the risks of acrylamide:

- **Children**: Due to their lower body weight and potentially higher intake of acrylamide-rich foods relative to body size, children may be more vulnerable to its effects.

- **Pregnant Women**: Acrylamide can cross the placenta, potentially affecting fetal development.

- **Individuals with Genetic Susceptibility**: Variants in genes related to acrylamide metabolism may increase susceptibility to its toxic effects.

1.2.7 Summary of Health Risk Levels

Risk Category	Evidence in Animals	Evidence in Humans	Confidence Level
Carcinogenicity	Strong	Limited/Inconclusive	Moderate
Neurotoxicity	Strong	Weak	Moderate
Reproductive Effects	Moderate	Weak/Unknown	Low-Moderate
Chronic Conditions	Emerging Evidence	Emerging Evidence	Low-Moderate

2. Chapter 2 - Health Risks Associated with Acrylamide Exposure: Outcomes of WG3/WG5 discussion

This chapter was developed based on round table discussions during the Zagreb joint WG3/WG5 workshop held on the 9th of April 2024 in Zagreb

2.1 Clarifying the Health Risks Associated with Dietary Intake of Acrylamide

Goal: Demonstrate unequivocally whether acrylamide is a matter of concern in humans.

- **Rationale:** Over 20 years on from the discovery of acrylamide in foods, the adverse effect on humans is still not confirmed.
- **Background:** High levels of acrylamide exposure, especially through industrial or occupational settings, can affect the nervous system, causing symptoms such as muscle weakness, numbness, and coordination issues. Acrylamide is also classified as a probable human carcinogen (Class 2a) however, evidence is based on animal studies at high doses. Even so, MOE for those with high acrylamide diets is estimated to be 50 (recommended maximum levels usually allow for an MOE of 1000. Also, there is doubt if the MOE approach, which assumes a linear dose response, is valid for acrylamide as the dose/response for acrylamide is proven to be hypolinear in animal and human studies. However, epidemiological studies, which are limited, show no link between acrylamide and cancer. Some evidence shows links with renal and ovarian cancers. One reason put forward is that detoxification of acrylamide seems to occur more rapidly in humans than in rodents, depleting acrylamide and reducing the potential to form glycidamide. Glycidamide is known to form adducts with DNA, however this is a minor reaction compared to other reactions occurring *in vivo*, all suggesting that acrylamide may be less harmful in humans. Evidence of carcinogenicity in humans is still inconclusive.
- **Approach:** Epidemiological studies need to be complemented with *in vitro* and *in vivo* toxicology. It is important:
  - to further our understanding of the mechanism and underlying biochemistry/ toxicology of acrylamide,
  - to further explore the "bioaccessibility" of acrylamide (how much is released from the food, how much is removed by other components of the diet) since the same dose of dietary acrylamide exposure results in very different absorption in the human body
  - to explore the bioavailability (how much is digested, absorbed and available for conversion to glycidamide). With a relatively short half-life in the body, what is the potential for DNA adduct formation?
  - and to evaluate the MOE approach for acrylamide in view of the previous.

- This needs a collaborative, concerted and multidisciplinary approach from academia, research organisation and industry. From ACRYRED's point of view, we need more toxicologists to join the Cost Action.

2.2 Risk impact modelling

Goal: Modelling the risk associated with acrylamide consumption

- **Rationale:** The primary reason for conducting risk impact modelling is to quantify and predict the actual impact of acrylamide exposure on public health, allowing for a more data-driven approach to risk management. By assessing potential health risks associated with various acrylamide levels, risk impact modelling provides a foundation for making informed decisions on setting regulatory limits and developing tailored industry practices. It also enables us to balance and prioritise health and safety objectives with practical considerations in the food production chain, contributing to a more focused, efficient, and scientifically grounded approach.
- **Approach:** Engagement with experts in human biology, toxicology, neurobiology, epidemiology and risk impact modelling for a broad range of cereal-based products. This is a long-term project and requires more detailed mitigation information across the supply chain and across the cereal-based product portfolio.

2.3 Awareness of Acrylamide

Goal: To provide a balanced view of acrylamide to all sectors of the population.

- **Rationale:** Whilst the jury is out on the potential harm caused by acrylamide, there is a need to spread awareness and minimise acrylamide in food products to as low as is reasonably achievable (ALARA – current legislation brought in 2017) or to comply with benchmark limits (proposed by the EU commission for 2024). After obtaining more conclusive toxicological proof of the toxicity of acrylamide in humans followed by the EU regulation of acrylamide levels with Maximum Levels, Public Awareness campaigns are required to inform consumers.
- **Background:** There are diverse views on the possible adverse effects of acrylamide on human health, ranging from those who lobby for tighter regulations and maximum limits, to those who have no awareness, and those who don't care.
- **Approach:** Acquisition of data across Europe, collected from surveys. These can be targeted at the general population to determine their awareness of acrylamide and their perception of the relative risk compared to other known risks. It should also include perceptions of risk and attitudes of those in the baking sector.

3. Conclusion

This strategy is designed to address the potential health risks of acrylamide in food by both prioritising long-term research on the potential harm to humans because of dietary acrylamide, and implementing immediate reduction measures for use by industry, food service and home use.

At the core of this strategy is a commitment to understanding the potential carcinogenic risks of acrylamide. While acrylamide is classified as a probable human carcinogen, its impact at typical dietary levels remains inconclusive. Animal studies suggest a risk, yet epidemiological evidence in humans is lacking and biochemical markers indicating potential toxicity provide so far, no evidence. To address this knowledge gap, a multidisciplinary research effort combining toxicology, epidemiology, and risk impact modelling is essential.

Future Research Directions

To better understand the health implications of acrylamide, future research should focus on:

1. Long-term epidemiological studies to clarify its role in human cancer and other diseases.
2. Investigations into genetic and metabolic differences affecting individual susceptibility.
3. Improved analytical methods to accurately measure dietary exposure levels.
4. Development of biomarkers to assess acrylamide-related health risks more effectively.

Acrylamide's presence in common foods necessitates a cautious approach to dietary intake and further exploration of its health effects.

In balancing the immediate need for risk reduction with a commitment to long-term research, this strategy positions the food industry to provide safer products while addressing evolving health concerns. The overall ACRYRED strategy will take a holistic approach to production, considering all stages from pre-harvest to processing, to address acrylamide formation factors in a way that spans the entire food chain.

Acrylamide in foods remains a public health concern due to its potential carcinogenic and neurotoxic effects. While typical dietary exposure levels are unlikely to pose immediate health risks, cumulative effects over a lifetime warranty precautionary measure. Reducing acrylamide exposure through informed cooking practices and industry innovations is crucial for minimizing health risks. Ongoing research and monitoring are essential to better understand its long-term effects and to develop more effective mitigation strategies.

References

- International Agency for Research on Cancer (IARC)
- European Food Safety Authority (EFSA)
- World Health Organization (WHO)