HEAT-INDUCED CONTAMINANTS

Safe sizzling

Dangerous substances from the pan, the deep fryer and the oven: heating causes changes in unprocessed foods or ingredients. It makes them easier to digest and they taste better. But heating also results in undesirable chemical compounds. Do these compounds pose a problem to health?

The first chemical compounds harmful to health that occur when food is prepared at high temperatures were detected in grilled fish and meat in the 1970s. The compounds in question were polycyclic and heterocyclic aromatic hydrocarbons. Since this time, we have made quantum leaps in our knowledge regarding potentially hazardous substances in heated foods, and several hundred of these heat-induced contaminants have meanwhile been identified. The most well-known of them are acrylamide, furan, monochloropropandiol and glycidol. These substances are addressed on the following pages.


© Cornelius M. Braun

Only four out of many

The "fatal four" represent only a small fraction of the undesirable substances that are created when foods are heated. Nothing or only very little is known about the potential risk to health of many of the other substances that may be formed. Scientists at the BfR therefore want to fill these gaps in our knowledge with the help of novel computer-assisted toxicological methods (see the interview on page 12). So that suggestions can be provided to the risk management experts as to which substances should take priority when new regulations are introduced. The aim is to identify further compounds that might give rise to a particularly high or difficult-to-manage health risk. A further focal point of research is to clarify the toxic effect mechanisms of undesirable substances that are already known. Moreover, the BfR scientists intend to develop methods that permit more precise calculation of the actual exposure of humans to these compounds (see info box). These methods will make it possible to further improve assessment of the health risk of these undesirable substances.


© Cornelius M. Braun

What really ends up in the body

What amount of heat-induced contaminants from foods is actually ingested via the intestine? Using the example of glycidyl fatty acid esters, the BfR showed in a research project that the determination of adducts in the blood is a suitable biomarker of measuring the quantity of contaminants that is actually present in the body – the "internal exposure" – more accurately. Adducts are composite molecules. In the body, glycidol is split off from the glycidyl fatty acid esters. Glycidol bonds with the blood protein haemoglobin to form a glycidol adduct. In the BfR study, test persons ate a defined amount of a commercially available palm fat daily with a known concentration of glycidyl fatty acid esters over a period of four weeks. During this time, the glycidol adduct level in the blood of the test persons almost quadrupled compared to the original level based on everyday intake. The data can be used to calculate the current level of this everyday intake.

Acrylamide: the monomer from the kitchen

The discovery of acrylamide in foods was a coincidence. Acrylamide is in fact a building block – a monomer – of the plastic material known as "polyacrylamide". But then researchers in Sweden found acrylamide not only in the blood of workers who had been contaminated with the synthetically produced plastic component due to a work accident, but also found this same chemical compound in the blood of people who had not been involved in the accident. In 2002, the scientists searching for the cause of this contamination made an important discovery, when they found that foods like crispbread, toasted bread, chips, crisps, roast potatoes, roasted cereals and coffee also contained significant amounts of acrylamide. But how did this molecule find its way into potatoes and bread?

© Wavebreakmedia/iStock

Acrylamide is a product of the "Mailliard reaction", a chemical reaction that occurs when we bake, roast, fry or deep fry raw foods – in other words, when we heat them to temperatures in excess of 120 degrees Celsius. Two of the things that happen is that the foods in question become brown and taste different than before. Acrylamide is created during this process when starch, sugar and certain amino acids react with each other in the absence of water. The darker a product becomes during heating, the higher the acrylamide content.

Toxicological tests to determine the effect of this substance in the body showed: acrylamide changes the genetic material (genotoxic effect) and causes cancer in various organs and tissues (carcinogenic effect) when administered to rodents in high doses. These effects are mostly caused by a metabolite of acrylamide, named glycidamide.

Since the chemical compound was first detected, scientists at the BfR have been assessing the health risk of foods containing acrylamide. The problem is that, due to their genotoxic-carcinogenic properties, it is not possible to define a safe intake amount for heat-induced contaminants. This is why there have been efforts for a number of years now to reduce acrylamide levels in foods based on the ALARA principle. The acronym ALARA stands for As Low as Reasonably Achievable. It means that ready-to-eat foods should contain as little acrylamide as is technically achievable with reasonable effort. Based on a BfR risk assessment, the risk management authorities developed a signal value concept in Germany from 2004 onwards, and this resulted in a significant reduction in acrylamide levels in industrially produced foods. In 2018, the Acrylamide Regulation of the European Union stipulated binding guide values for different food groups based on what is achievable in line with the current state of the art. The food and catering industries must comply with these stipulated levels.

Consumer tip

When preparing foods like roast potatoes, biscuits, toast and chips, don't let them get too brown. "Golden not charred" should be the motto in order to minimise acrylamide in the kitchen.

The BfR acrylamide calculator measures how much acrylamide we ingest every day with our food: www.bfr.bund.de/cm/343/acrylamidrechner.xls

© Floortje/iStock

Furan: canned foods and co.

Furan is a highly volatile chemical compound and is mainly found in roasted coffee, canned foods, baby food in jars and ready meals. It is created in substantial amounts when carbohydrates, amino acids, ascorbic acid (vitamin C) and unsaturated fatty acids react with each other during roasting and when foods are heated in closed containers.

Animal studies on rats and mice show that furan causes benign tumours and leukaemia as well as liver and testicular cancer in high doses. The underlying mechanisms have not yet been identified. It is therefore not clear whether and to what extent these effects are of relevance to humans. Although the European Food Safety Authority (EFSA) estimates that a massive 90 percent of the furan ingested by adults in Europe comes from coffee, epidemiological studies show that cancer rates among coffee drinkers are no higher than among people who do not drink coffee at all. In view of the major gaps in data on both effects on human health and exposure, it is not possible to definitively assess the health risks of furan.

In view of these uncertainties, it is advisable to minimise the intake of furan to the greatest possible extent. A BfR working group conducted a research project to determine how the way coffee is prepared or the methods by which ready-to-eat foods are heated can reduce the furan level in the meals on our plates. They found that the furan content falls by up to 66 percent if canned soup is heated in open pans or bowls. The furan remained in the foods in the case of ready meals with low water content and a more solid texture. They also found that espresso from the machine contains far more furan than conventional filter coffee – despite the fact that the raw material (ground coffee) had the same furan content in both cases.

Consumer tip

Prepare meals and baby food yourself from fresh raw products. Heat ready meals (canned soups) and jars of baby food in a pan without a lid while stirring. Enjoy coffee in moderation, and preferably drink filter coffee.

Monochloropropandiol and glycidol: Two hazardous by-products of edible oil processing

Until 2007, 3-monochloropropandiol (3-MCPD) had only been detected in soy sauce or bread, but that was the year when tests conducted by the monitoring authorities of Germany's federal states made major waves. It was found that industrially produced infant formulae, the basic foodstuff for babies who aren't breastfed, contained 3-MCPD fatty acid esters. The main source of these heat-induced contaminants are refined oils and fats from the oil palm. These contaminants are formed when the untreated oils from the plant are treated using superheated steam during the refining process in order to remove bitter substances as well as other undesirable aromatics and suspended solids (deodorisation). Long-term studies have shown that 3-MCPD in high doses causes tumours in the kidneys, testicles and mammary glands of male rats. The mechanism behind tumour formation is not yet fully understood, but it is assumed that the compound does not have any mutagenic effects. This means it was possible to determine a value at which no carcinogenic effect is to be expected based on current knowledge. The BfR used this research to derive a tolerable daily intake (TDI) of 2 micrograms 3-MCPD per kilogram bodyweight. This value has meanwhile been confirmed by other authorities like EFSA.

Until recently, it was not clear whether this toxic effect can also be expected in the case of the fatty acid esters of 3-MCPD and the chemically related 2-MCPD. In these compounds, the 2-MCPD or 3-MCPD is firmly bound to fatty acids. Two BfR studies showed that this bond is broken by the process of digestion in the gastrointestinal tract. This results in the formation of free 2-MCPD and 3-MCPD. It is therefore to be assumed that the intake of these fatty acid esters carries the same health risk as intake of the free substances.

Glycidol and glycidyl fatty acid esters are also created during the refining of vegetable oils. This means that they are also contained in the fats and edible oils obtained from these vegetable oils. Unlike MCPDs, free glycidol damages the genetic material. If glycidol is added to the feed of rats in high doses over a lengthy period of time, the animals develop tumours. Due to its genotoxic-carcinogenic properties, it is not possible to derive a safe intake level for glycidol. As is the case with acrylamide, therefore, foods should contain as little as possible of this chemical compound. This also applies to glycidyl fatty acid esters, from which glycidol is released in the gastrointestinal tract and which should therefore be assessed as being equivalent to glycidol from a toxicological point of view.

Consumers cannot influence the level of 2-MCPD and 3-MCPD, glycidol and their fatty acid esters in foods that have already been processed or in food ingredients like oil and fat. This must be done by the producers of refined vegetable fats and oils – by taking suitable measures during the production and processing of palm oils and during the deodorisation process to reduce the levels of these contaminants in their products. At the same time, however, this range of substances can also be formed at home if vegetable oils or fats are heated in the kitchen during frying and come into contact with salted foods. ◘

Confounding of cellular protective mechanisms

In animal experiments, 3 and 2-MCPD were shown to damage kidneys and testicles, and to promote tumours. In a joint project with the Fraunhofer Institute for Toxicology and Experimental Medicine, the BfR has discovered a new mechanism on the molecular level of the cells that relates to this effect. In an animal study, the substances were administered to rats. Modern biochemical methods were used to investigate how the cells in the liver, kidneys and testicles of the animals form, alter and regulate proteins under the influence of 3-MCPD and 2-MCPD ("Proteomics"). It was found that the protein DJ-1, which is known to have an antioxidative effect in the cells, is inactivated by the substances. In the protein formation process, DJ-1 normally suppresses the undesirable influence of readily reactive oxygen molecules that disrupt cellular functions. The BfR showed that 3-MCPD and 2-MCPD permanently change the DJ-1 protein by combining it with oxygen – and that the protein loses its protective function as a result. Consequently, the cells are exposed to oxidative stress; new proteins are incorrectly formed. Current knowledge indicates that oxidative stress is involved in various diseases, including cancer and Parkinson's.

Consumer tip

Only add salt to vegetables, fish and meat after frying or use or unsalted marinade.

Professor Dr. Dr. Alfonso Lampen studied Biology and Biochemistry in Göttingen as well as Veterinary Medicine (majoring in Pharmacology and Toxicology) in Hannover, where he also obtained a postdoctoral qualification in Food Toxicology. His core field of research is the intake, transformation, and transport of food-related foreign substances in the gastrointestinal barrier and the investigation of toxic mechanisms on molecular level in the cells. He lectures in Food Toxicology at The University of Veterinary Medicine Hannover, Foundation (TiHo).

"We can use computer models to find out whether a substance damages our DNA"

Toxicology 4.0: computer-assisted methods are increasingly being used in the field of regulatory toxicology to identify the toxic properties of substances. Professor Dr. Dr. Alfonso Lampen, Head of the Food Safety Department at the BfR, talks about the use of "computer-assisted toxicology" in research into food safety.

Professor Lampen, computer-assisted systems have long been used in pharmacology in the identification of chemical compounds that are suitable for use as active substances in medications. You take the opposite route. What does the BfR do exactly?

We are looking into the benefits of these computer systems known as *in silico* models for the prediction of the health-damaging properties of heat-induced contaminants and other undesirable substances. We intend to use these methods to filter out from the wide range of undesirable substances those substances that might potentially be mutagenic or carcinogenic. The modelling concepts and simulations help us to prioritise experimental investigations.

What is the basis for these *in silico* models?

We compare chemical structures – or, more precisely, structural activities, in other words the interaction of certain molecule structures with biological systems. In the case of *in silico* models, these kinds of chemical structures that are known from experiments to exhibit certain cell-damaging properties are stored in databases. These include chemical structures that alter genetic material and can therefore have a mutagenic effect or interfere with biochemical processes in the cells in other ways and cause cancer. We compare the known, defined structures with the structures of the individual substances whose effects we currently know little about. The information we obtain about their structure indicates whether they might possess toxic properties.

What is special about the way the *in silico* models are used at the BfR?

There are other research groups working with these methods. What's new about our approach, however, is that we combine the various existing methods and models and then apply them to food-related contaminants in order to arrive at more robust statements regarding the potency of these contaminants. In the case of genotoxicity, in other words changes to genetic material, we have combined five different software tools, and we combined three for the carcinogenicity test.

Which contaminants did you investigate?

In a research project, we first looked at the heat-induced contaminants that have not yet been investigated. There are more than 800 substances that can be created when foods and their raw materials are heated. The project was designed to establish whether and to what extent *in silico* methods are suitable for predicting whether a particular substance has a genotoxic or carcinogenic effect. This was indicated by the software tools on a scale from 0 to 1. Values between 0.66 and 1 signalled a high probability of genotoxic or carcinogenic properties, while values below 0.66 did not provide any clear pointers.

And what were your findings?

From more than 800 heat-induced contaminants, our approach has enabled us to identify 24 that are highly likely to have a genotoxic effect based on their structure or based on components of their structure. These 24 contaminants are right at the top of the priority list for further experimental testing.

Where you surprised by your findings?

There are naturally some substances and structures whose genotoxic effect was already known from experimental analysis – substances such as aldehydes, for example. But there were also substance groups for which no experimental data is currently available – such as thiazoles – that were identified as genotoxic with a high degree of probability. The study showed that the models for the identification of genotoxicity are very suitable, as we were able to conduct follow-up experimental analysis that confirmed the predictions of the models. In other words, computer models can help us to find out whether a substance can damage our genetic material.

And what is the situation with carcinogenicity tests?

The predictive capacity of the models is not yet particularly high in this area, but this is only natural, as the development of cancer is a very complex process. Chemical compounds may play a role in the creation of a tumour; they can promote the growth of a tumour or cause inflammation that changes the properties of the cells, thereby promoting the development of a tumour. This is why it is difficult to model the toxicological endpoint of carcinogenicity. It's not clear whether we will be able to develop suitable *in silico* models for this purpose at all.

What are the next steps in the application of these systems at the BfR?

It is important to consider the conversion of heat-induced contaminants in the body and to incorporate the relevant parameters in the computer models. We know from cell-based and animal experiments that parent substances that are not genotoxic-carcinogenic can be converted in the body into metabolites that can have genotoxic or carcinogenic effects because they possess a specific structure. We can already simulate the creation of new chemical structures in the metabolic process today using *in silico* methods. Our next goal, therefore is to combine these methods with *in silico* methods for toxicological analysis.

Mr. Lampen, many thanks for the interview. ◘