Bundesinstitut für Risikobewertung (BfR)

Updating the risk assessment of acrylamide in foods

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At the end of April 2002 the Swedish National Food Administration reported research findings on acrylamide in various foods. What were, in some cases, very high levels, caused concern. BgVV (now BfR), therefore, convened an expert hearing already in May 2002 and has been working on this problem since then. At the beginning of August 2002 the first step taken to reduce the risk involved the proposal of an "action value" for acrylamide in foods. It has since been supplemented with signal values for specific product groups. Both types of value aim to reduce the levels of acrylamide in foods.

Different levels of risk to the consumer from eating acrylamide-containing foods have been estimated. Some of the repeatedly raised questions and points, which led to a need for discussion, are taken up once again and discussed here.

Dangerous properties of acrylamide

The main harmful property of acrylamide is its carcinogenic effect. It was detected – as is customary when examining chemical substances – during animal experiments in long-term studies in rats. In these animals, acrylamide induced the formation of malignant tumours in several organs. The lowest dose which induced tumours when administered daily was 1 to 2 milligram per kg body weight in rats.

Concerning other harmful effects of acrylamide, like damage to the nervous system ("neurotoxicity") or the impairment of fertility, it can be assumed that no significant risk occurs from the amounts of acrylamide taken up from food.

Can the carcinogenic effect detected in the animal experiment be transferred to the situation for man?

The transferability of dangerous effects, which were found in animal experiments, to man is one of the major problems of toxicology. There are two main issues when it comes to acrylamide:

1. Is acrylamide also carcinogenic in man?
2. Can the effect detected at a dose of 1 to 2 milligrams per kg body weight also occur at lower doses?

These two questions are discussed below. We can already say at this stage that according to the current state of scientific knowledge, it can be assumed that acrylamide taken up from food can also be carcinogenic in man.

(1) Is acrylamide also carcinogenic in man?
It goes without saying that not all the details of the effect of acrylamide can be directly transferred from animals to man. However, knowledge about the uptake of acrylamide from food into the body, its distribution in the body organs, degradation, excretion and biological effects in the cells do not supply any indications that acrylamide would behave in a fundamentally different manner in the human body from the way it does in the rat.

Hence, acrylamide is classified in category 2 of carcinogenic substances in the European legal system. This means that it should be considered as carcinogenic for man. The substances in category 1 of this classification have been proven to have a carcinogenic effect in man. Epidemiological studies are required in order to detect the carcinogenic effect

of substances in man. Here, the incidence of cancer in individuals who were exposed to a chemical substance is compared with the incidence of cancer in persons who were not exposed to that same substance. Epidemiological studies are available for acrylamide in which the incidence of cancer did not differ between the two groups. Nevertheless, the all clear cannot yet be given. This is because a moderate increase in cancer incidence in the group of individuals exposed to acrylamide could only be detected if the study involved a very large number of people. The non-detection of a carcinogenic effect is not, therefore, proof of the non-occurrence of this effect.

(2) Can the effect detected at a dose of 1 to 2 milligrams per kg body weight also occur at lower doses?

In the animal experiments to test for the carcinogenic properties of acrylamide, doses were used – as is customary in tests – which were high but still tolerable. These doses are far higher than the amounts taken up from food by man. This raises the question: Are the effects identified at high doses also of relevance for this low dose range?

When describing a risk from the angle of the amount of substance taken up, "quantitative risk description", it is of decisive importance in the case of carcinogenic substances whether they also have a genotoxic effect, i.e. can damage the genotype. In this case the majority of scientists use the "threshold concept":

- For non-genotoxic carcinogenic substances it is assumed that a specific dose must first be exceeded before this effect occurs. It is assumed that below this dose there is no heightened risk of cancer (so-called threshold value or threshold dose).

- By contrast, in the case of genotoxic substances it is assumed that each (even low) uptake involves an increased risk of cancer. In the simplest case, the risk increases in direct relationship to the amount taken up. This is then called a linear dose-response relationship. Because of the unreliable data situation, it is frequently impossible to determine in the low dose range whether there is a deviation from the linear dose-response relationship. It is, however, assumed that this is probably frequently the case.

These assumptions are generally accepted in scientific circles. In exceptional cases a deviation can be made from these assumptions. For this, scientifically backed substantiation is required. What is the situation for acrylamide?

The genotoxic effect of acrylamide

Extensive studies are available on the genotoxic effect of acrylamide. In mammalian cell cultures (in vitro) and in animal experiments (in vivo), acrylamide has genotoxic effects. From the toxicological angle, the inheritable changes to genotype (mutations) are particularly relevant amongst the genotoxic effects. There are three relevant types: gene mutations: chromosome mutations and chromosome nondisjunctions (aneuploidies). Acrylamide induces chromosome mutations. Apparently, gene mutations are not induced. It was not specifically investigated whether aneuploidies are also induced.

In line with the general basic assumption for genotoxic substances, a mechanism without a threshold value is taken as the basis for the genotoxic effect of acrylamide. Mechanisms are indeed conceivable which lead to a threshold dose for genotoxic substances, too. A threshold mechanism is, for instance, plausible for substances which solely induce aneuploidies. This possibility was discussed by various groups for acrylamide. Given the clear induction of chromosome mutations, the sole induction of aneuploidies can clearly be ruled out.

Some experts have undertaken theoretical considerations which do not justify any "real threshold" but which could provide indications of a non-linear dose-response relationship. In fact, the mode-of action for the genotoxic effect of acrylamide – as is the case with most

genotoxic substances – has not been clarified in detail. Because of the major importance of these issues, BgVV commissioned a research project in order to examine how the dose-effect response behaves in the low dose range.

Exposure: Amounts taken up

The derivation of the cancer risk from acrylamide in foods is rendered more difficult by the fact that only inaccurate estimates are available about the amount taken up. This has to do firstly with the fact that acrylamide was found in very many foods and that the measurement values for various foods in a group may vary considerably. Secondly, scarcely anything is known about the eating habits of various groups in the population. In order to clarify this situation, BgVV launched a study in which the eating habits of 16-year-old school pupils are to be examined. Given their consumption of what are, in some cases, highly contaminated product groups like potato crisps and chips, this group is of particular interest.

This paper does not intend to enter into a detailed examination of the different exposure assessments but to merely make the following comment. Various assessment assume that the average exposure to acrylamide in foods is in the range of 0.3 to 1 milligram per kg body weight and day. It is clear that there are major differences between groups in the population and individual groups of the population are probably far higher than 1 milligram per kg body weight.

How high is the risk of cancer?

Today, the cancer risk from acrylamide in foods cannot be reliably quantified. Various approaches were adopted in order to describe the level of the risk:

- It was pointed out that the carcinogenic potential of acrylamide in rats is comparable with that of other known carcinogens, e.g. 3,4-benzopyrene. This comparison is of relevance because the level of 3,4-benzopyrene in foods is subject to very strict regulations.

- Some assessment institutes undertake calculations with the help of mathematical models in order to draw conclusions from the cancer rates found in animals experiments about the probability of cancer in man. For comparative considerations an exposure dose of 1 microgram per kg bodyweight and day is normally used ("unit risk"). The lifelong intake of such a dose – as explained above – is in a realistic range for acrylamide. Depending on the model, this would lead to a risk of between 700 and 10,000 cases of cancer per one million people. Already the major variability reflects the uncertainty of the evaluation. At the same time, it is clear that even the lower value in the given range of risk evaluation would be very high.

- An alternative approach compares the dose, which is carcinogenic in animals, with the amount taken up by man. According to comments by Professor Schlatter, Federal Health Agency in Switzerland, at a BgVV information event on acrylamide on 29 August 2002, a rough estimate for acrylamide leads to a factor of 1,000 [by way of explanation: the lowest carcinogenic dose in the animal experiment is 1,000 times higher than the estimated uptake for man.]. If one compares this "safety margin" of 1,000 with the corresponding factors for other carcinogenic substances, then it is relatively low.

- In principle, the ALARA principle applies to genotoxic and carcinogenic substances. ALARA is the abbreviation for "as low as reasonably achievable".

For the Federal Institute for Risk Assessment, these considerations lead to the conclusion that acrylamide exposure through foods must be drastically reduced as soon as possible.

Statistical versus individual risk

In order to realistically estimate the risk from acrylamide and to communicate this in an understandable manner, it is essential that this be placed in a suitable context. The comparisons given above are helpful in this respect. Furthermore, the distinction between the statistical and the individual risk, which must be assessed differently, is of particular importance. In order to illustrate this, let us assume that a substance would increase the cancer rate in man by 0.5%, i.e. through the regular uptake of this substance 5 out of 1,000 people would develop cancer. In order to keep the example simple, it should be assumed here that Germany has a population of 80 million with an average age of 80. Related to the population (statistically) this would mean that in Germany every year 5,000 cases of cancer could be avoided if exposure to the substance were prevented. From this angle, the substance clearly constitutes an unacceptable risk. The individual risk is considered in a different way. The basic risk of developing cancer during one's lifetime is on average 20 to 25% for the German population. A contribution of 0.5% to this risk would, therefore, be relatively small compared to the basic risk.

What is important for efficient risk communication is that the risks are clearly presented. Unfortunately, at present consumers do not have enough information about the acrylamide burden in individual foods. A series of recommendations has already been elaborated which, besides the possible abstention from entire product groups, offers individuals ways to reduce their exposure to acrylamide in foods. The recommendations are available, for instance, from the AID Acrylamide Forum.