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The Food Safety–Nutrition Nexus

The focus of this issue of *Cereal Foods World* is food safety, so this column will address one of the issues where there is a nexus between nutrition and food safety. There are many such issues, including the following: 1) use of salt to promote growth of beneficial organisms and desirable fermentation in the preparation of yeast bread, cheese, and sausage and reduce growth of pathogenic microorganisms. Salt, however, has become a concern because the amount consumed in the diets of 95% of Americans is at the Upper Level established by the Institute of Medicine. High levels of sodium increase the risk for stroke and elevated blood pressure in salt-sensitive individuals. 2) Removal, soaking, or trimming of the peel and seed coats of fruits, vegetables, and grains can lower the levels of heavy metals, pesticides, aflatoxins, and other toxins, many of which are more likely to occur in these outer layers. However, these outer layers also contain many nutrients and phytochemicals, and their removal lowers the level of nutrients delivered by a food. Removal of these layers also may call into question a grain's "whole-grain" status. 3) In some cases, cooking temperatures and times that are associated with optimal product quality and flavor and that ensure the destruction of harmful organisms may cause a significant loss of nutrients or lessen the availability of nutrients such as thiamin and heme iron. Heating may also increase the production of heterocyclic amines and other heat-produced products, such as acrylamide, which have been indicated as possible mutagens and carcinogens.

This column explores the acrylamide issue in light of nutritional recommendations to make grain-based foods the base of a diet and to increase dietary-fiber and whole-grain intakes. Thus, for the cereal industry, acrylamide is an important example of the nexus between nutrition and food safety.

Acrylamide Intake and Food Safety

Carbohydrate-rich foods that contain some protein, such as breads and cereals, can form acrylamide when exposed to temperatures higher than 120°C. Grain-based foods, as well as some vegetables (e.g., asparagus and potatoes), that are parched, popped, fried, baked, roasted, or extruded can form acrylamide as a result of the reaction between carbohydrates, especially glucose and fructose, and the amino acid asparagine. The preparation of ready-to-eat breakfast cereals, crackers, toast, snacks, and cookies to optimize their color, flavor, and texture through the Maillard reaction can also cause the formation of acrylamide. Grain-based foods are dietary contributors of acrylamide for consumers in all age groups because they can be found in nearly all meal segments and many snack items in the Western diet. In a European survey published in April 2011, soft bread was the third highest acrylamide contributor for adults, children, and adolescents (6).

Food products have only recently been recognized as a source of acrylamide. Prior to 2002, human contact with acrylamide was thought to be due only to industrial exposure. Swedish investigations into a tunnel-construction accident showed that persons not involved in the accident or exposed to acrylamide in the work place had indications of acrylamide exposure. This led to the supposition and subsequent documentation that food products were a source of exposure. This reality not only stunned consumers, the food industry, and regulators, but also sparked a worldwide coordinated effort to assess the risk acrylamide from food sources poses to humans. Based on early findings, in 2009 the European Chemical Agency listed this compound among substances of very high concern. WHO classified it with the group of chemicals "thought to have no reliably identifiable threshold." (Such a classification means that very low concentrations may result in a less than one in a million risk, but the substance does not have zero risk.) Risk assessments carried out by the Joint FAO/WHO Expert Committee on Food Additives concluded that acrylamide may be a human health concern. Thus, in 2007 the European Union initiated a three-year survey to monitor intake data. Worldwide efforts on the part of academics, industry, and regulators have resulted in a number of strategies that can reduce exposure to acrylamide through foods.

When the acrylamide story broke in 2002, there was no research on the health impacts of this compound from food consumption, even though the compound must have been present since humans started using fire in the preparation of foods. Since 2002, much effort has been made to look for potential health impacts, and the results of many of these analyses are finally being published. This column discusses some of the findings on the health risks of consumption of acrylamide from foods, with a special focus on grain-based foods and how this issue fits within the food safety–nutrition nexus.

Acrylamide as a Carcinogen

Industry studies show that acrylamide from industrial (work place) exposure can cause neurological problems. The studies agree that high levels are needed and that such problems are unlikely to occur through food exposure. However, it has been suggested that mutagenic and genotoxic changes, through the formation DNA adducts (reaction of acrylamide or its metabolite glycidamide), may arise from the levels of acrylamide found in food sources. Thus, both animal and epidemiological studies investigating possible links between acrylamide in foods and various cancers have been undertaken.

Breast Cancer. The findings for studies attempting to link acrylamide and breast cancer differ. Some animal studies show

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consistent results indicating acrylamide in drinking water increased cancer of the mammary gland, while others show no effect of acrylamide in the drinking water of prepubertal F344 rats (1,17). Most human studies show either a lack of association, weak association, or association in a specific subset of the population. Results from the U.K. Women's Cohort Study ($N = 33,731$ women aged 35–69 years) show that acrylamide intake, estimated from a 217-item food frequency questionnaire, was not associated with the risk for breast cancer in the cohort considered in its entirety. Subdivision of the cohort indicated a weak positive association between dietary acrylamide intake and breast cancer in premenopausal women but not in postmenopausal women (3). Results for the U.S. cohort differ. In the Nurses' Health Study, there was no association between acrylamide intake and breast cancer risk in the 88,672 women studied (19). Data segmentation of the U.S. cohort by menopausal status and smoking habits (smoking also contributes to the body load of acrylamide) did not alter the findings. Thus, these prospective studies show no clear relationship between acrylamide and breast cancer, and if there is a risk, it is small and affects only a subset of the population.

Lung, Pancreatic, and Brain Cancers. The Finnish Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study of more than 27,000 male smokers aged 50–69 years, shows that acrylamide slightly increased lung cancer risk among smokers (7). The relative risk (RR) of the highest versus the lowest quintile of acrylamide intake was 1.18. While there was a slight increase in the risk for lung cancer in this cohort of male smokers, no other cancers showed an association with acrylamide intake. Similarly, there was no association between acrylamide intake and pancreatic cancer in a case-control study in northern Italy with 326 patients and nearly twice as many controls (15). No relationship between acrylamide and brain cancer was found in a 5,000-person subset in the prospective Netherlands Cohort Study on diet and cancer. Although the human epidemiological data are encouraging, some concerns remain, because an animal trial with acrylamide administered in the drinking water caused an increase in central nervous system tumors in rats (10).

Ovarian and Endometrial Cancers. Studies show the least concordance regarding ovarian and endometrial cancers. In the Nurses' Health Study, there was an association for an increased risk for endometrial cancer among those consuming high levels of acrylamide (19). The authors also report that there was a nonsignificant increased risk for ovarian cancer overall but a significant increase in risk for serious ovarian tumors (RR = 1.58).

In the Netherlands Cohort Study on diet and cancer, the risk for ovarian and endometrial cancers was higher for those in the highest quintile of intake compared with those in the lowest quintile of intake (9). For those in the quintile ingesting the most acrylamide and who never smoked, the risk for ovarian cancer nearly doubled. However, these findings do not agree with those from the Swedish mammography cohort of 61,057 women over 60 years of age. In this cohort there was no association between acrylamide intake and ovarian or serious ovarian cancer (11). Comparison of the studies shows that the women in the Dutch study were of ages similar to those in the Swedish study, but one study used quintiles and the other used quartiles. The intakes in the highest quintile in the Dutch cohort were 40.2 μg/day compared with 32.5 μg/day in the highest Swedish quartile. The lowest quintile intakes in the Dutch study were 8.9 μg/day compared with 15 μg/day in the lowest quartile of the Swedish cohort. Thus, the range of intakes between the highest and lowest was 31 μg/day in the Dutch study, which employed quintiles, compared with 16.9 μg/day in the Swedish study, which employed quartiles. Both groups love coffee, which is an important contributor to acrylamide intake in the diets of adult Europeans (6). The Dutch also eat honey cake for breakfast (a type of gingerbread), and gingerbreads contain among the highest acrylamide levels of measured foods. Two different conclusions were drawn by the authors of recent reviews on the effect of acrylamide on ovarian cancer risk. A meta-analyses published in 2011 concludes there is no association between ovarian cancer and acrylamide intake (16). Another review suggests, however, there is an increased risk for ovarian and endometrial cancers associated with acrylamide intake (8,9).

The 2011 meta-analysis by Pelucchi et al. (16) is based on the results of 25 human studies. It shows no increase in cancer risk for any cancer with an increase of 10 μg of acrylamide per day. The RR ranged from 0.98 for esophageal cancer to 1.01 for colon, endometrial, ovarian, and kidney cancers. Thus, the authors conclude there is no increase in risk from acrylamide exposure from foods. However, this same meta-analysis shows a significantly increased risk for pancreatic and kidney cancers due to industrial exposure.

The conclusions drawn from the meta-analysis of human data by the Italian group differ from those of a review published by Hogervorst et al. (8) at Maastricht University in Holland. This review considers both animal and human data and shows increased risks for ovarian and endometrial, renal cell, estrogen (and progesterone) receptor-positive breast, and oral cavity cancers for nonsmoking women. Their review shows inverse associations for lung and bladder cancers in women and prostate and oro- and hypopharynx cancers in men. The authors of the Dutch review suggest that rodent models may not be the best models for predicting cancers and that more studies are needed with respect to mechanism.

In terms of mechanisms, some authors have looked at DNA adducts on hemoglobin as a mechanism by which acrylamide may impact cancer risk. One large U.S. analysis, using a subset of the National Health and Nutrition Examination Survey database with 7,000 adults, shows a positive correlation with DNA adducts, but the correlation is small (18).

In short, the available data indicate there may be some increase in the risk for some cancers, but in most cases, the increase is small and limited to those consuming very high levels of acrylamide.

The Acrylamide–Food Safety and Nutrition Nexus

Epidemiological studies, primarily on Western diets, show that diets containing grains, whole grains, and cereal fiber are associated with a lower risk for disease and disease mortality. For instance, a Nordic study shows that whole-grain rye bread was associated with lower mortality risk (12). Similarly, the National Institutes of Health–American Association of Retired Persons cohort, composed of 388,000 participants ages 51–70 years, shows that those in the quintile who ate the most cereal fiber, compared with those in the quintile who ate the least, had significantly lower total mortality at any age (14). In terms of cancers, there are studies showing that whole grains, specifically whole-grain breads, were associated with lower colon cancer risk in a Danish population (5). Some, but not all, studies show that intake patterns for white bread, red meats, potatoes, and traditional foods were associated with higher risks for some cancers. However, the Mediterranean diet, which also is high in breads, was associated with lower risks for many cancers in a number of studies. Thus, studies of diet pattern may not shed light on the dietary effects of acrylamide from foods such as breads and cereals, partly due to confounding effects, or they may show the effects of other foods on mutagenicity and genotoxicity potential of acrylamide. Rat studies indicate that other dietary constituents, such as resveratrol, sulfur compounds from vegetables, and polyphenolics from tea, inhibit capacity of acrylamide to form DNA adducts (20). This suggests that studies on acrylamide from food sources should be looked at in the context of the total diet.

There are many compounds produced by the Maillard reaction, so a focus on only one heat-produced compound among many may fail to show the impact of acrylamide from a food matrix with a complicated mix of chemicals, some of which have been shown to have antioxidant and other beneficial properties. For example, pronyl-lysine is found in bread crust and is produced during high-temperature baking of bread. This compound is a potent free-radical–scavenging antioxidant that exerts chemopreventive activity by reducing oxidative stress (13). When animal studies administer acrylamide in drinking water and not in the form in which it is actually obtained from the diet, these studies may not be relatable to acrylamide formed in foods that contain other chemicals. One study in experimental animals that compares acrylamide from bread crust to acrylamide in drinking water shows that the crust slightly reduced acrylamide bioavailability (2).

Dietary guidelines commonly place grain-based foods at the base of the diet, and there is substantial data showing the positive health impacts of breads and cereals, particularly those which contain whole grains and are high in fiber. Further research is needed to show how acrylamide consumed as part of normal foods in the diet may be countered by diets adequate in fiber, nutrients, phenolics, and Maillard browning products that may inhibit adduct formation and that comprise the recommended diet.

Conclusions

An analysis of the food safety–nutrition nexus affirms strategies for both industry and consumers. There must be continuance of collaboration among industry, academia, and government to reduce the acrylamide content of foods without adversely impacting the quality of the product or introducing other nutritionals risks. For industry, strategies such as those described in the CIAA (Confederation of the Food and Drink Industries of the EU) Acrylamide Toolbox (4) to optimize frying and baking times, remove asparagine though enzymatic or breeding techniques, change the availability of reducing sugars, and optimize leavening systems are among the techniques that could be employed. For consumers, the best strategy is to concentrate on meeting nutritional guidelines and eat an adequate amount of grains, cereal fiber, and whole grains as the basis of their diet. Since large numbers of consumers fail to meet such recommendations, a focus on what to eat, which has been shown to improve quality of life and reduce health risks, may be a more productive effort than concentrating on risks that are possible but much smaller and may be countered by proper food selections.

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