Review of Methods for the Reduction of Dietary Content and Toxicity of Acrylamide

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Potentially toxic acrylamide is largely derived from heat-induced reactions between the amino group of the free amino acid asparagine and carbonyl groups of glucose and fructose in cereals, potatoes, and other plant-derived foods. This overview surveys and consolidates the following dietary aspects of acrylamide: distribution in food originating from different sources; consumption by diverse populations; reduction of the acrylamide content in the diet; and suppression of adverse effects in vivo. Methods to reduce adverse effects of dietary acrylamide include (a) selecting potato, cereal, and other plant varieties for dietary use that contain low levels of the acrylamide precursors, namely, asparagine and glucose; (b) removing precursors before processing; (c) using the enzyme asparaginase to hydrolyze asparagine to aspartic acid; (d) selecting processing conditions (pH, temperature, time, processing and storage atmosphere) that minimize acrylamide formation; (e) adding food ingredients (acidulants, amino acids, antioxidants, nonreducing carbohydrates, chitosan, garlic compounds, protein hydrolysates, proteins, metal salts) that have been reported to prevent acrylamide formation; (f) removing/trapping acrylamide after it is formed with the aid of chromatography, evaporation, polymerization, or reaction with other food ingredients; and (g) reducing in vivo toxicity. Research needs are suggested that may further facilitate reducing the acrylamide burden of the diet. Researchers are challenged to (a) apply the available methods and to minimize the acrylamide content of the diet without adversely affecting the nutritional quality, safety, and sensory attributes, including color and flavor, while maintaining consumer acceptance; and (b) educate commercial and home food processors and the public about available approaches to mitigating undesirable effects of dietary acrylamide.

KEYWORDS: Acrylamide; food processing; food safety; reduction; cereals; potatoes; coffee; diet; toxicity

INTRODUCTION

Foods are processed for a variety of reasons: to render them edible if they are not; to permit storage; to alter texture and flavor; and to destroy microorganisms, undesirable enzymes, and other toxins (*1–4*). Processing methods include heating (baking, cooking, frying, microwaving), freezing, aging, and exposure to acidic and basic conditions. Although processing of foods can improve nutrition, food microbiology, quality, and safety, these processing alternatives can occasionally lead to the formation of toxic compounds. These consequences of food processing result from molecular interactions among nutrients and with other food ingredients, both natural and added. An improved understanding of the molecular changes during food processing and the resulting nutritional and safety consequences is needed to optimize beneficial effects such as food quality, bioavailability, and food safety and to minimize the formation and facilitate the inactivation of deleterious compounds. Such insights will encompass multidisciplinary studies of the plant physiology, chemistry, biochemistry, nutrition, and toxicology of food ingredients.

A number of research needs related to the reduction of potentially toxic acrylamide levels in the diet have been previously described (*5–17*). This overview comprehensively surveys and interprets present knowledge of worldwide efforts to define the distribution of acrylamide in the food chain and to reduce acrylamide levels in processed foods. The information and suggested research outlined below may facilitate and guide further needed studies to reduce acrylamide content of the diet to improve food safety as well as human health.

Tables 1–5 and **Figures 1–15**, prepared from published data, are illustrative of experimental findings that are relevant to acrylamide mitigation of the diet. The depicted tabular data and illustrations are designed to facilitate understanding of the dietary sources of acrylamide consumed by people of different ages and in different countries and to explore some of the preharvest, postharvest, and in vivo approaches that can be used to reduce acrylamide levels of different food categories. Continuing worldwide efforts to define dietary acrylamide levels originating from different counties are described in refs *18–35*.

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Table 1. Summary of Acrylamide Intake Estimates for Food Consumed in the United States [a] (Adapted from Reference *265*)

food	acrylamide (ppb = μg/kg)	intake range (μg/day)
almonds (fried or roasted)	320	0.05–0.93
bagels, untoasted	31	0.28–0.43
biscuits	37	0.15–2.37
bread (soft breads, all types)	**31**	**1.00–1.69**
white bread	11	0.29–0.77
wheat bread and whole grain	39	0.43–2.38
cake	10	0.09–1.00
cereal, ready-to-eat (all types)	**86**	**1.99–4.88**
corn flakes[b]	**61**	**1.41–3.46**
crisped rice[b]	**56**	**1.29–3.18**
granola[b]	**51**	**1.18–2.89**
oat rings[b]	**174**	**4.02–9.87**
cereal, cooked; oatmeal; grits; cream of wheat	0	0.00–0.00
cereal, cooked, Wheatena	738	?[c]–30.3
chicken nuggets/breaded chicken	24	0.21–?[c]
chile con carne	**130**	**1.05–?**[c]
coffee (brewed)	**7**	**1.71–3.73**
cookies (all types)	**188**	**2.37–7.76**
sugar cookies[d]	41	0.52–1.69
graham crackers[d]	**459**	**5.78–19.0**
chocolate chip cookies[d]	**130**	**1.64–5.40**
corn chips/tortilla chips	199	0.80–9.15
crackers	167	0.63–3.17
doughnuts	18	0.07–0.85
French fries	**413**	**5.00–26.3**
olives, canned	414	0.28–4.14
pancakes and waffles	15	0.08–1.29
peanuts, roasted	27	0.04–0.55
peanut butter, total	88	0.31–2.99
pie	22	0.15–3.56
pizza	20	0.38–3.50
popcorn	180	0.47–4.32
potato chips	**466**	**2.47–14.4**
Postum (dry), wheat-based coffee substitute	4573	0.01–13.7
prune juice	159	0.09–16.4
quick breads and muffins	8	0.05–0.70
sunflower seeds	39.5	0.01–1.15
sweet potatoes, canned	84	0.06–26.0
toast	**213**	**1.64–7.31**
tortillas (corn or flour)	6	0.04 – 0.41

[a] Source of food consumption data: CSFII 94−96, 98 survey where possible; otherwise, intake rates are based on CSFII 94−96 (*266*). Bold font indicates foods for which the range of average daily intake exceeds 1.0 μg/day. Intake range is the mean per capita intake (lower bound) to the mean intake if one ate the food every day (upper bound). [b] Intake estimates for cereal subtypes assume a person eats that type of cereal solely. [c] Intake data are unavailable. [d] Intake estimates for cookie subtypes assume a person eats that type of cookie solely.

DISTRIBUTION OF ACRYLAMIDE IN FOOD CONSUMED BY DIFFERENT POPULATIONS

Acrylamide in food is largely derived from heat-induced reactions between the amino group of the free amino acid asparagine and the carbonyl group of reducing sugars such as glucose during heating (baking, broiling, frying, roasting). Foods rich in both of these precursors are largely derived from plant sources such as potatoes and cereals (barley, rice, wheat) but apparently not from animal foods such as poultry, beef, and fish. **Figure 1** depicts proposed mechanistic pathways leading to the formation of acrylamide from asparagine and reducing sugars (*36–41*). A different mechanism operates for the formation of acrylamide from lipids (*42*), a less significant source of acrylamide. Widely consumed processed foods with high levels of acrylamide include French fries, potato chips, tortilla chips, bread crust, crisp bread, various baking goods cereals, and coffee. Although the source of food, for example, potatoes, is important, because observed acrylamide amounts vary widely even within a particular food, other factors may be equally

Table 2. 2006 U.S. FDA/CFSAN Exposure Assessment for Acrylamide (Top 20 Foods by Mean Acrylamide Intake), July 2006 [Adapted from Di Novi (*136*)]

food	mean acrylamide intake (μg/kg of bw/day)	cumulative percentile[a]
French fries, from restaurants	0.070	0.16
French fries, oven baked	0.051	0.28
potato chips	0.045	0.38
breakfast cereal	0.040	0.47
cookies	0.028	0.53
brewed coffee	0.027	0.60
toast	0.023	0.65
pies and cakes	0.018	0.69
crackers	0.017	0.73
soft bread	0.014	0.77
chile con carne	0.014	0.80
corn snacks	0.011	0.82
popcorn	0.007	0.84
pretzels	0.007	0.86
pizza	0.006	0.87
burrito/tostada	0.006	0.88
peanut butter	0.003	0.89
breaded chicken	0.003	0.90
bagels	0.003	0.90
soup mix	0.003	0.91

[a] Sum of first column = 0.91, which is the end of the second column.

important. For example, acrylamide concentrations of chips prepared from Korean potatoes ranged from 408 to 3241 μg/kg (*27*). Wide variations in amounts of acrylamide in different food categories as well as in different brands of the same food category (e.g., cereals, French fries, potato chips, coffee) appear to result not only from variability of the precursor levels present both naturally in selected cultivars and as a result of postharvest handling but also from differences in processing conditions (e.g., pH, temperature, time, nature of food matrix).

Acrylamide is ubiquitous in the food supply. **Tables 1–3** and **Figures 2–4** show consumption levels of acrylamide from various foods and food categories. There are wide variations in levels among populations from different countries and also among specific groups (children, adolescents, adults, men, and women) (see **Figure 2**). Moreover, the range within a population also varies widely (see **Figure 3**). The fifth percentile gets most of their 0.1 μg/kg of body weight (bw)/day of acrylamide from bread, whereas for the 95th percentile, with intake levels at 1.5 μg/kg of bw/day, bread is a minor contributor (7%) in a diet high in a variety of processed and refined foods. Although detailed discussions on the trends in acrylamide levels shown in the graphic and tabular data are beyond the scope of this paper, the observed large variation of total dietary acrylamide levels contributed by different food categories should stimulate the development of additional approaches to reduce acrylamide content of high-acrylamide foods. We agree with the suggestion (*14*) that at this time, public health measures for reducing acrylamide in the diet should focus on the highest potential impact foods, not on reducing the mean acrylamide intake. We should base our efforts where they would have the greatest impact: reducing acrylamide in foods that are both a dominant source of acrylamide for some populations and most widely consumed.

For the American diet based on ~2500 samples evaluated, the results show that 100% of the population consumes some acrylamide as part of the diet, with a mean intake of ~0.4−0.5 μg/kg of bw/day. No significant differences in the mean intake were seen in three exposure assessments carried out from 2003 to 2006. This is also the case for subsets of Hispanic, Asian, or southern regional consumers.
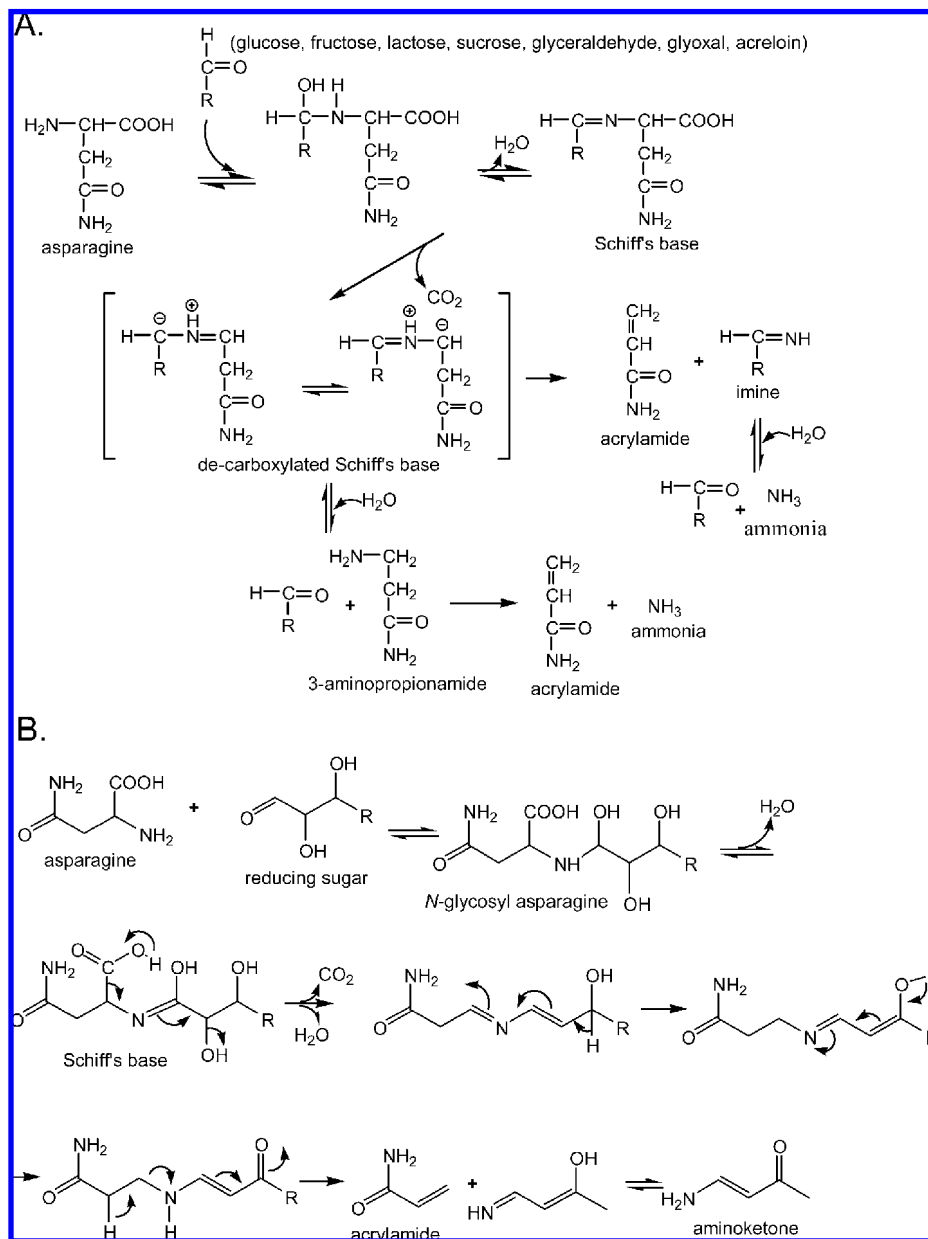
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Figure 1. Mechanisms of acrylamide formation in heated foods: (**A**) transformation of asparagine and a carbohydrate to a decarboxylated Schiff base, which is then further transformed to acrylamide directly and/or via the 3-aminopropionamide intermediate; (**B**) by contrast, the indicated electron flow leads directly to acrylamide without the formation of the 3-aminopropionamide intermediate. Adapted from refs *36–41*.

FACTORS THAT MINIMIZE ACRYLAMIDE CONTENT IN FOOD

We will now address, with some overlap, efforts designed to achieve reduction of acrylamide in several specific food categories. For convenience, the 30 parameters that have been evaluated are listed in **Table 4**. Separately, we examine possible approaches to mitigating the in vivo toxicity of acrylamide. In the last section, we outline research needs in all of these areas.

Reduction of Acrylamide Content of Cereal Products. Figure 2 shows that although cereals are a major dietary source of acrylamide, the percentage of total acrylamide that cereals (bread, cereals, and crackers, cookies, cakes) contribute varies for different populations, ranging from ∼24% in the diet of Swedish adults to ∼44% in the diet consumed by Belgian adolescents, with the American diet at 40%. The following are some of the reported efforts designed to reduce the acrylamide content of cereal grain-derived foods.

Agronomic–Genetic Factors. Asparagine levels in wheat grown under conditions of severe sulfate depletion were up to 30 times greater as compared to levels in wheat grown in soils with sufficient amounts of sulfate fertilizer (*43*). This was also reflected in observed acrylamide levels of baked products. Levels in products prepared from high-asparagine wheat flours ranged from 2600 to 5200 μg/kg and those from wheat grown under normal conditions, from 600 to 900 μg/kg. These observations suggest the need to develop new wheat varieties with low asparagine content and that wheat should be either be grown in soils with adequate amounts of sulfates or that the soil should be amended to provide adequate sulfates to the crops.

The acrylamide content of breads largely depended on the wheat cultivar used to prepare the dough (*44*). Levels were related to free asparagine and crude protein content. Nitrogen fertilization of the soil induced elevated amino acid and protein contents, resulting in increased acrylamide levels in breads.
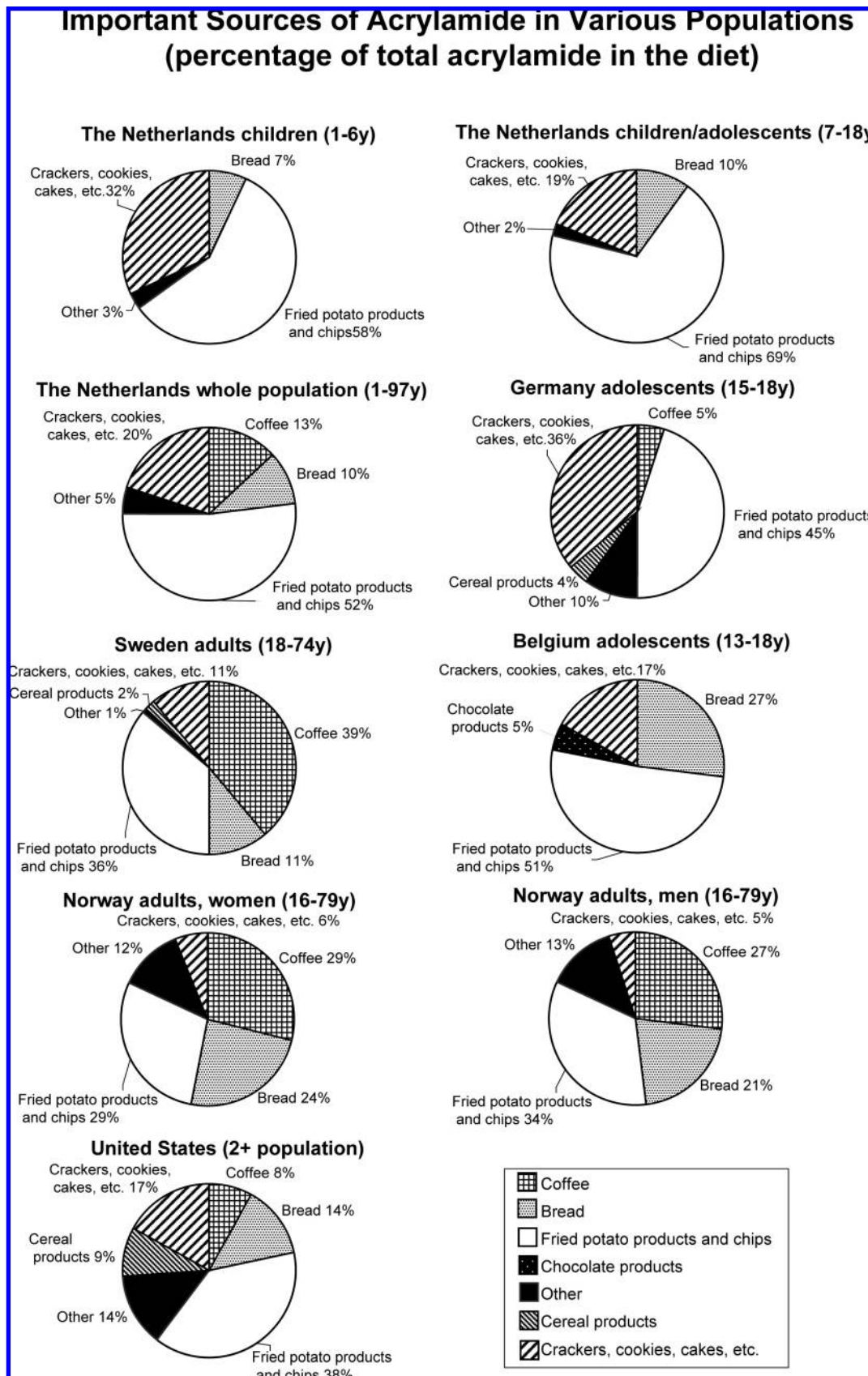
Important Sources of Acrylamide in Various Populations
(percentage of total acrylamide in the diet)

The Netherlands children (1-6y)
Crackers, cookies, cakes, etc.32%
Bread 7%
Other 3%
Fried potato products and chips58%

The Netherlands children/adolescents (7-18y)
Crackers, cookies, cakes, etc. 19%
Bread 10%
Other 2%
Fried potato products and chips 69%

The Netherlands whole population (1-97y)
Crackers, cookies, cakes, etc. 20%
Coffee 13%
Bread 10%
Other 5%
Fried potato products and chips 52%

Germany adolescents (15-18y)
Crackers, cookies, cakes, etc.36%
Coffee 5%
Fried potato products and chips 45%
Cereal products 4%
Other 10%

Sweden adults (18-74y)
Crackers, cookies, cakes, etc. 11%
Cereal products 2%
Other 1%
Coffee 39%
Fried potato products and chips 36%
Bread 11%

Belgium adolescents (13-18y)
Crackers, cookies, cakes, etc.17%
Chocolate products 5%
Bread 27%
Fried potato products and chips 51%

Norway adults, women (16-79y)
Crackers, cookies, cakes, etc. 6%
Other 12%
Coffee 29%
Fried potato products and chips 29%
Bread 24%

Norway adults, men (16-79y)
Crackers, cookies, cakes, etc. 5%
Other 13%
Coffee 27%
Fried potato products and chips 34%
Bread 21%

United States (2+ population)
Crackers, cookies, cakes, etc. 17%
Coffee 8%
Bread 14%
Cereal products 9%
Other 14%
Fried potato products and chips 38%

Legend:
⊞ Coffee
▒ Bread
☐ Fried potato products and chips
⬛ Chocolate products
■ Other
▨ Cereal products
▧ Crackers, cookies, cakes, etc.

Figure 2. U.S. data obtained from a table developed by Office of Environmental Health Hazard Assessment, California Environmental Protection Agency (OEHHA) (*265*). They combined data from the Appendix: FDA Data on Acrylamide Concentration in Foods (*26*) and from food consumption data in the Continuing Survey of Food Intakes by Individuals (CSFII) 94−96, 98 survey (USDA) when possible; otherwise, intake rates were based on CSFII 94−96 (*266*). Other country data were obtained from Dybing et al. (*277*). Foods were recategorized into broader groups to provide consistency when different cultures were compared. Spice biscuits, biscuits, Dutch spiced cakes, cookies/biscuits/wafers, prepared toast, crisp bread, crackers, and crisp bread/thin unleavened bread were all combined into one category for simplicity. Other categories include other snacks, special snacks, roasted nuts, and popcorn.

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Table 3. Acrylamide per Portion for Selected Foods Consumed in the United States[a] (Adapted from Reference *136*)

food	acrylamide (μg/kg)	portion size[b] (g)	acrylamide (μg)/portion
brewed coffee	7.8	240	1.9
canned black olives	242.8	15	3.6
breakfast cereal	119.4	55	6.6
potato chips	597.5	30	17.9
Postum, brewed	93	240	22.3
French fries, restaurants	404.1	70	28.3
prune juice	214.4	140	30.0
French fries, oven baked	697.8	70	48.8

[a] The 2006 Exposure Assessment for Acrylamide, Michael DiNovi, Ph.D., FDA/CFSAN, July 2006. [b] Portion sizes from 21 CFR 101.12.

These ranged from 10.6 to 55.6 μg/kg. Harvest year, climate, and sprouting of the grain also affected acrylamide contents of breads.

Soil fertility, agronomic, and genetic approaches for reducing levels of acrylamide precursors (asparagine, reducing sugars) in cereal and potato plants (discussed below) are active areas of investigation (*45–47*).

Bread Baking and Toasting. **Figures 5** and **6** highlight trends in acrylamide formation in cereals and breads. Studies by Surdyk et al. (*48*) showed that (a) >99% of acrylamide formed during baking of breads is found in the bread crust; (b) the acrylamide level of the crusts was related to temperature and time of baking; and (c) the surface color of the crust strongly correlated with acrylamide content. The lack of acrylamide in the bread crumb is not surprising, in view of the fact that the internal temperature of bread crumb does not exceed 100 °C during baking (*49, 50*). The acrylamide content of toasted bread slices increased with toasting time (*51*). Dark toast made from potato bread had a high amount of acrylamide (>600 μg/kg). To minimize acrylamide content, consumers should avoid toasting bread to a "dark" stage and scrape the surface to remove the dark parts of toasts and other baked goods (*51*).

Effect of Sodium Bicarbonate. The baking agent ammonium bicarbonate (NH_4HCO_3) promotes acrylamide formation in sweet bakery products (**Figure 6**). Acrylamide formation was lowered by replacing it with sodium bicarbonate ($NaHCO_3$) (*52*). Not surprisingly, the promoting effect of the ammonium salt appears to be due to its ability to enhance the formation of reactive α-dicarbonyl intermediates, which then combine with NH_3, forming sugar imines that are then transformed to acrylamide.
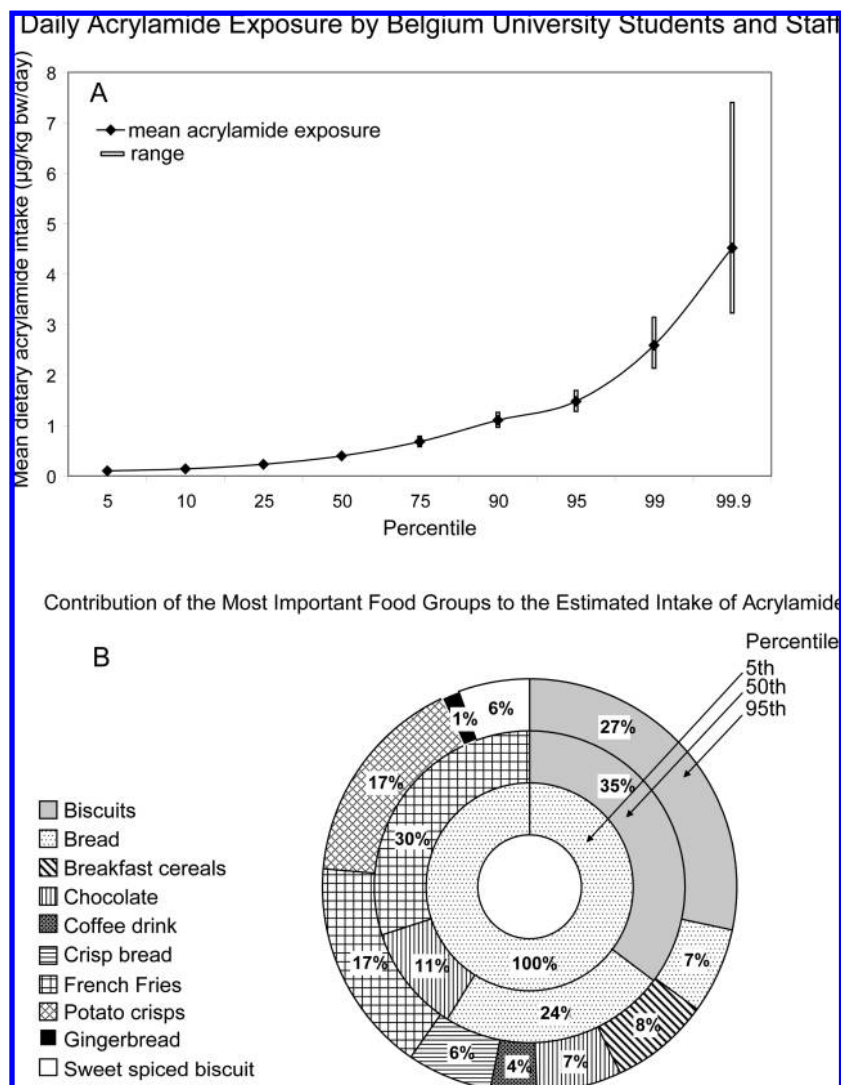

Figure 3. (**A**) Variability and uncertainty of the dietary acrylamide intake (μg/kg of bw/day) (best estimation [90% confidence interval]). (**B**) Contribution of the most important food groups to the estimated intake (mg/kg of bw/day) of acrylamide [best estimation (% on total exposure)]. Adapted from Mestdagh et al. (*19*).
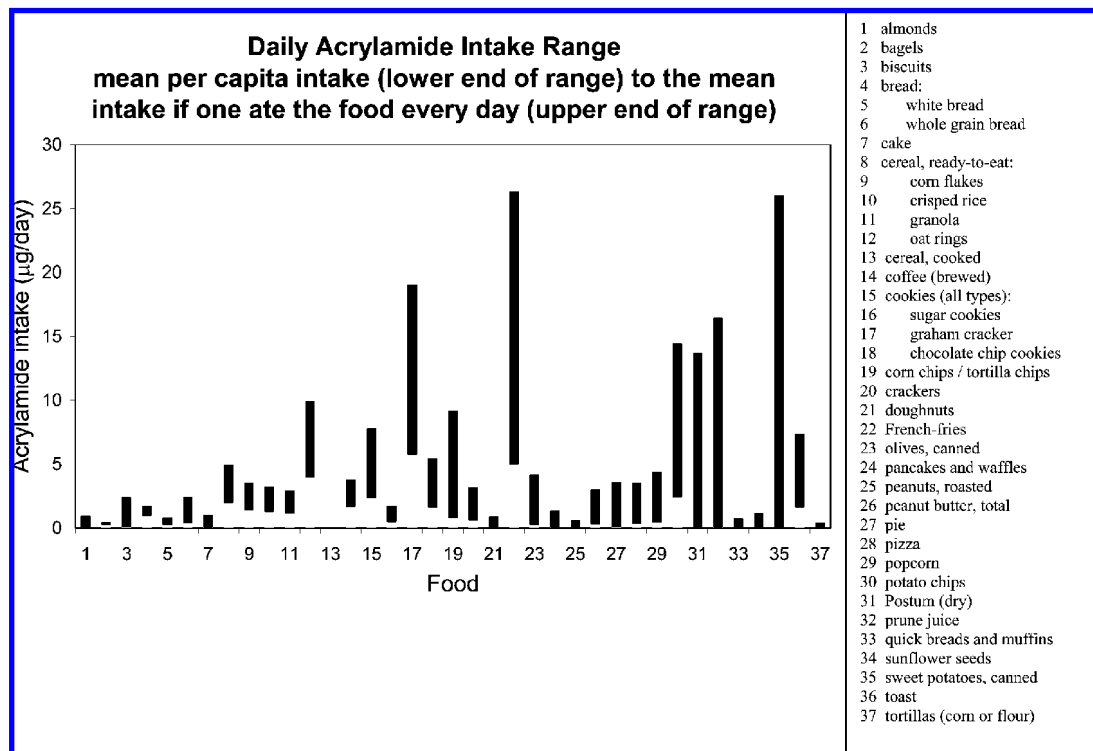
Figure 4. Created with data from the Office of Environmental Health Hazard Assessment/California Environmental Protection Agency, 2005 (*265*).

Effect of Glycine. Mitigating effects of added amino acids on acrylamide levels of heated glucose/asparagine mixtures are shown in **Figure 7A,B**, of bread crust and flatbreads in **Figure 7C,D**, and of potato chips in **Figure 7E,F**. The following wide-ranging amounts of acrylamide were present in baked cereal products (in µg/kg): crisp bread, 54; butter cookies, 179; heated flour, 2004; and gingerbread, 2381 (*53*). The acrylamide content of wheat breads with added asparagine increased up to 3640 µg/kg. Added glycine decreased acrylamide concentrations (*54*). The authors suggest that spraying glycine on the surface of fermented dough can lead to a significant reduction of acryla-mide content of yeast-leavened breads. The higher the asparagine content of the dough is, the greater the reduction rate.

Because lysine is nutritionally found in insufficient amounts in cereals (*49, 55–57*), it would be of interest to find out whether adding lysine to flours or doughs would result in increased lysine content as well as reduced acrylamide levels of breads. However, the use of lysine may significantly increase the extent of browning. This could possibly be exploited if other methods of acrylamide mitigation that reduce browning are employed, such as cooking at a lower temperature, thus creating products acceptable to the consumer as well as of high nutritional quality.

Effects of Sucrose and Trehalose. The following examples indicate that reducing sugars are an essential precursor for the acrylamide reaction. Replacing inverted sugar and honey in the recipe with the nonreducing sugar sucrose resulted in a 20-fold decrease in acrylamide formation in gingerbread (*58*). Adding the nonreducing disaccharide trehalose (currently used in many commercial food applications) to glucose/asparagine or ascorbic acid/asparagine mixtures inhibited acrylamide formation, pre-sumably by suppressing the generation of the intermediate carbonyl compounds such as pyruvaldehyde (*59*). Significantly less acrylamide was formed in cookie doughs containing sucrose compared to glucose (*60*). However, when the pH of the doughs was lowered by the addition of citric acid, the acrylamide content was decreased in glucose-containing doughs, but unexpectedly increased in sucrose-containing doughs, presumably due to hydrolysis of sucrose to the reducing sugars glucose and fructose. These results indicate that replacing the reducing sugars glucose and fructose with the nonreducing sugars sucrose or trehalose may mitigate acrylamide formation.

Asparaginase and Other Enzymes. Studies by Weisshaar (*61*) showed that (a) asparagine content of the raw materials is the limiting factor in acrylamide formation of baked products; (b) other baking ingredients, especially almonds, contributed to the acrylamide content of the products; and (c) treating potato, rye, and wheat flours with the enzyme asparaginase resulted in a 96% hydrolysis of asparagine to aspartic acid in the dough as well as in low acrylamide levels in baked goods prepared from these doughs.

The beneficial findings with asparaginase suggest that other enzymes may be effective in modifying acrylamide precursors, including commercially available glucose oxidase that catalyzes the oxidation of glucose.

A complementary approach would be to use so-called acrylamidinases (or other enzymes) to hydrolyze acrylamide in food to acrylic acid (CH_2=CH−COOH) and ammonia or to otherwise metabolize the molecule to nonreactive and safe products (*62*). Although to our knowledge such enzymes are not currently available, they could be produced by recombinant DNA techniques. For example, it may be possible to explore bacterial strains of *Rastonia eutropha* TDM-3, reported to denitrify (metabolize) up to 1446 mg/L acrylamide from wastewater (*63*). Large-scale production of the enzyme respon-sible for the metabolism of acrylamide could be accomplished by preparing a genomic DNA library of the *Rastonia* micro-organism, screening the library for activity, isolating the gene responsible for activity, expressing the gene in *Escherichia coli*, and then purifying and characterizing the expressed enzyme (*64*). It would also have to be shown that such enzymes are safe to consume.

Effect of Yeast Fermentation of Dough. **Figure 5D** shows that fermentations of wheat and rye doughs result in significant
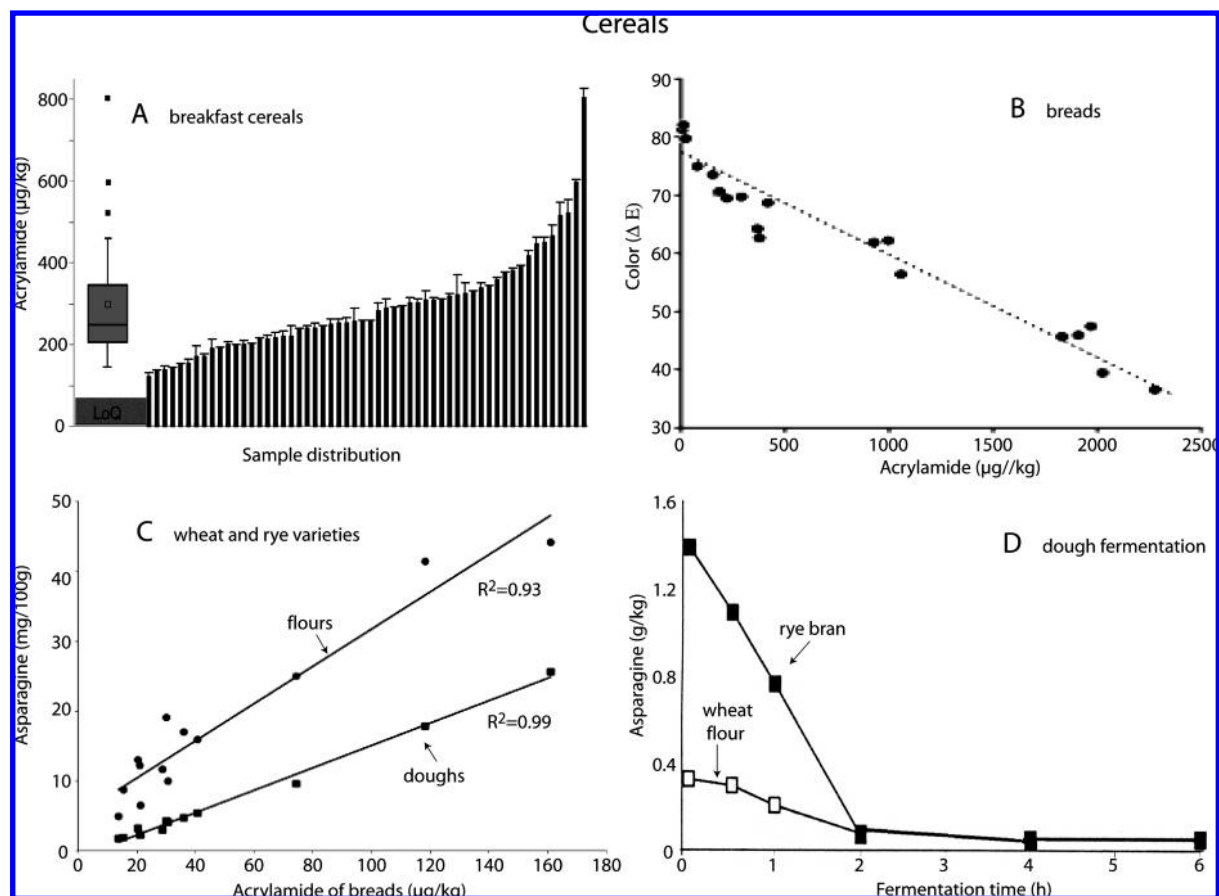
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Figure 5. (**A**) Bar graph and box-and-whisker plot of acrylamide content in commercial breakfast cereals. Adapted from ref *278*. (**B**) Relationship between color (ΔE) and acrylamide content (μg/kg of dry crust) in breads from the temperature/time experiment using the same recipe with 0.1 g of asparagine added to 100 g of flour. A 0 represents black, and 100 represents white. Adapted from ref *48*. (**C**) Correlation of asparagine concentrations in flours (●) and doughs (▲) of different wheat, spelt, and rye varieties with the resulting acrylamide contents in produced breads. Adapted from ref *44*. (**D**) Free asparagine content before and after different fermentation times in doughs made from a 1:1 mixture of base flour and whole grain wheat flour (□) or rye bran (■). Adapted from ref *66*.

reduction in asparagine levels. Depending on the time and temperature used, the acrylamide content of yeast-leavened whole-grain rye crisp bread ranged from 10 to 30 μg/kg (*65*). Added asparagine increased the acrylamide content up to 349 μg/kg, whereas adding fructose to the flour had no effect. The authors suggest that the low levels in the rye bread they observed, compared to amounts up to 1900 μg/kg in some commercial rye breads, may be partly explained by the long fermentation time used. It is likely that most of the original asparagine transforms to other products during fermentation.

A related study reported similar results (*66*). Thus, prolonged fermentation of the whole-wheat dough resulted in an 87% reduction in acrylamide levels of breads as compared to a short fermentation time; the corresponding reduction for rye bread was 77%. Surprisingly, sourdough fermentation was less effective than yeast fermentation in reducing the asparagine content of the dough.

Effect of Microwaving of Popcorn. Microwaving of commercial popcorns (caramel sweet and cream salted) sold in China significantly lowered amounts of acrylamide compared to conventional heating (*67*). Acrylamide levels in these popcorns ranged from 146.5 to 2206 μg/kg. Reducing sugars present in the caramel sweet popcorn presumably contribute to the highest amount found in this heated product.

Meat−Cereal Combinations: Synergy in Acrylamide Formation. Paleologos et al. (*68*) determined acrylamide formation during cold storage of precooked (oil fried) breaded chicken products. Initial acrylamide concentrations of 910−970 μg/kg increased during a 23-day storage period to a maximum value of 1360 μg/kg for samples packaged under a modified atmosphere consisting of 60% CO_2−40% N_2 and to 1800 μg/kg in samples packaged under air. These observations indicate that the high initial acrylamide levels in breaded chicken products, likely resulting from the interaction between carbohydrates in the bread crumbs and free amino acids from the egg and chicken meat, increased even further during storage, especially storage in the presence of air. The authors suggest that the high level of acrylamide found in the precooked breaded chicken is a result of synergy between combinations of the food constituents exposed to a high temperature in the presence of oil. Will such synergy also result during the preparation of breaded fish products? It is not known why storage under an anaerobic atmosphere results in reduced acrylamide levels.
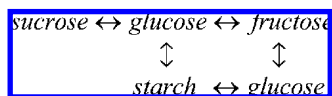
Reduction of Acrylamide Levels of Potato Products. Figure 2 shows that potato-derived foods constitute a major source of dietary acrylamide. The contribution of potato foods to total acrylamide intake ranges from ∼29% for adult Norwegian women to ∼69% (highest amount) for Dutch children/adolescents (7−18 years of age), with 38% the mean for the U.S. population. **Figures 7−12** summarize the results of extensive worldwide studies designed to discover ways to reduce acrylamide levels of processed potato products. Below, we examine some of the specific approaches designed to develop low-acrylamide potato products.

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Lowering the acrylamide precursors asparagine and/or reducing sugars glucose and/or fructose is expected to result in reduced acrylamide formation. The following studies show that the balance of the precursors may be just as important a factor, if not more so. Use of these methods to reduce acrylamide must take into account consumer acceptance and expectations of a certain amount of browning for desirable flavor, color, and texture.

Agronomic Factors: Plant Physiology. Ideally, breeding and/ or suppressing genes that encode enzymes governing the biosynthesis of free asparagine may achieve decreases in asparagine content. Selection from available varieties that contain low levels of asparagine for dietary use offers another approach to mitigate acrylamide content.

The findings by Elmore et al. (*69*) and by Muttucumaru et al. (*43*) show that for three potato varieties (a) low sulfur levels in the soil led to a decrease in acrylamide formation and in an increase in free amino acids and sugars; (b) elevated reducing sugar levels caused by the low-sulfur soils did not correlate with elevated acrylamide content; and (c) free asparagine levels as a proportion of the total free amino acid pool did correlate with acrylamide content. The authors propose that free asparagine as a percent of total amino acids is rate limiting. They suggest that when the sugar content is low, as it is in potato tubers, competition between asparagine and other amino acids for participation in the Maillard reaction may be a key determinant of the amount of acrylamide that is formed during processing. See also the earlier section on Agronomic–Genetic Factors.

Storage of Potatoes: Hydrolysis and Epimerization of Sugars. Sucrose, glucose, fructose, and starch are present in potatoes. Their proportions vary with postharvest treatment of the potato tuber. These potato ingredients participate in so-called coldsweetening induced hydrolysis and epimerization (inversion) reactions illustrated schematically as

$$
\begin{array}{ccc}
sucrose & \leftrightarrow \ glucose \ \leftrightarrow & fructose \\
& \updownarrow & \updownarrow \\
& starch \ \leftrightarrow & glucose
\end{array}
$$

The indicated pathways are cultivar-dependent and may be reversible. They can proceed in any direction. Above 10 °C, the sugars and starch remain in balance, with the free sugars either transforming into starch or being used up in other reactions. Below 10 °C, reducing sugars start to accumulate. The reducing sugars may participate in both nonenzymatic Maillard browning reactions and acrylamide formation during the processing of the potatoes. The reconditioning of potatoes at room temperature following cold storage, usually at 4 °C, results in significant reductions in the content of reducing sugars (**Figure 8B**).

Silva and Simon (*70*) found that for American potatoes (a) glucose, fructose, sucrose, and asparagine contents increased during storage of potatoes at 2 °C; (b) glucose and fructose but not sucrose or asparagine content correlated with subsequent acrylamide formation in the fried potatoes; (c) preconditioning of the tubers prior to storage at 2 °C by slowly lowering the temperature at a rate of 0.2 °C/day resulted in significantly reduced acrylamide levels in the fries; and (d) a higher rate of nitrogen fertilization resulted in increases in the free amino acid levels of the potatoes.

Matsuura-Endo et al. (*71*) found that during storage of Japanese potatoes for 18 weeks at 2, 6, 8, 10, and 18 °C (a) reducing sugar and acrylamide levels increased significantly at temperatures <8 °C, (b) levels of reducing sugars correlated with acrylamide levels for tubers with a ratio of fructose/

Table 4. Factors That Mitigate the Formation and Safety of Dietary Acrylamide

agronomy, plant genetics (*43–46, 69, 70*)
acidulants, pH (*105–108*)
amino acids (*53, 54, 106, 109–111, 113, 119, 120*)
antioxidants (*130, 131*)
atmosphere of processing (*91*)
asparaginase and other enzymes (*8, 11, 13, 267, 268*)
bioavailability, reduced (*127, 148*)
blanching and soaking (*92, 102, 103*)
bread toasting, light (*49*)
chemoprevention of toxicity
chick pea protein (*122*)
chitosan (*124*)
cultivar, variety (*53*)
fermentation, lactic acid (*104*)
fermentation, yeast (*65, 66*)
frying temperature (*72, 79, 80, 91, 92*)
glucose oxidase, proposed
ionizing radiation (*140, 269*)
metal ions (*124–126*)
microwaving (*139*)
moisture (*50, 88, 270*)
polymerization of acrylamide (*128, 271–274*)
precursor levels (*6, 28, 72–74, 78–84, 92*)
protein hydrolysates (*123*)
roasting temperature (*142, 143, 149, 150*)
sodium bicarbonate (*52*)
soil composition (*53, 69, 275*)
surface-to-volume ratios of potatoes (*74, 76*)
storage (*70, 71, 73, 74, 142, 143, 145, 149, 150, 276*)
sugars, nonreducing (*58*)

asparagine of <2; and (c) at ratios >2, asparagine rather than the reducing sugar content was the limiting factor for acrylamide formation. Related studies showed that (a) for Canadian potatoes, acrylamide formation during frying can be minimized by using tubers with low sugar content (*72*); and (b) asparagine levels in Swedish potatoes increased (*73*) and those of Japanese potatoes did not change during storage (*74*).

The cited studies indicate that potatoes grown in different parts of the world show different susceptibilities to compositional changes during storage.

Effect of Surface-to-Volume Ratios (SVR) of Potato Tubers. Matthäus et al. (*75*) found that in deep-fat-fried potatoes, acrylamide levels (a) increased following lowering of storage temperature of the tubers from 8 to 4 °C; (b) depended on the SVR of the potatoes; (c) correlated with reducing sugars ($r = 0.73$), but not with asparagine concentrations of the tubers or oil types used for frying; and (d) increased linearly with temperature up to 175 °C and nonlinearly with time of frying.

A related study on the influence of processing parameters on acrylamide formation during frying of potatoes (*76*) indicated that for potato tubers with a low SVR, acrylamide content consistently increased with increasing temperature from 120 to 230 °C as well as with time of frying, reaching maximum levels of 2500 μg/kg. By contrast, for potatoes with intermediate to high SVRs, maximal acrylamide formation of 18000 μg/kg for high SVR grated potatoes occurred at 160−180 °C. In the higher SVR potatoes, higher temperatures and longer processing times resulted in reduced acrylamide levels, perhaps an indication that the reaction for acrylamide formation is near completion, and further treatment leads to either degradation or other reactions. A correlation between acrylamide content and extent of browning was observed in low SVR and to a lesser extent in medium SVR potatoes. Although such correlations have been demonstrated by several other investigators (**Figure 9E−H**), these authors did not observe an acrylamide/browning
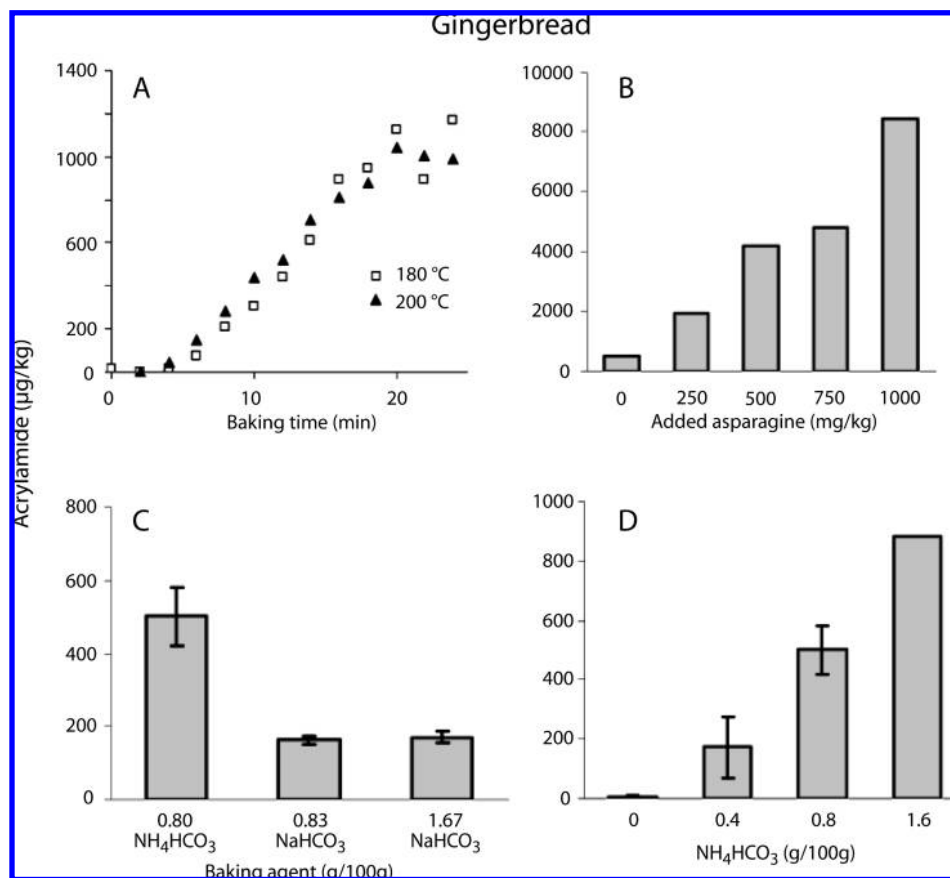
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Figure 6. (**A**) Influence of temperature and time on acrylamide formation during baking: (□) 180 °C; (▲) 200 °C. (**B**) Effect of added free asparagine on acrylamide formation in gingerbread. (**C**) Acrylamide contents in gingerbread with different baking agents. (**D**) Acrylamide content in gingerbreads produced with different amounts of ammonium hydrogen carbonate as baking agent. All adapted from ref *58*.

relationship for high SVR potatoes. Acrylamide content of low-fat potato snacks (489 µg/kg) was about one-third of values reported for potato chips (*77*).

Acrylamide Precursors in Commercial Potatoes. Biederman-Brem et al. (*78*) showed that (a) potatoes with <0.2 g/kg of fresh weight (fw) fructose and glucose are not suitable for roasting due to poor browning and flavor; (b) roasted products with >1 g/kg reducing sugars contain >500 µg/kg acrylamide; (c) to achieve lower acrylamide levels, potatoes used for roasting and frying should contain <1 g/kg of reducing sugars; (d) the latter level can be achieved by avoiding storage of fresh potatoes at 4 °C; and (e) a 250 g serving of hash browns or roasted potatoes may contain up to 1000 µg of acrylamide. Related studies by (*79, 80*) for potatoes grown in Switzerland showed that (a) fructose was twice as effective as glucose and 10 times more effective than lactose in generating acrylamide in potato and wheat flour; (b) frequent consumption of roasted, baked, or fried potatoes containing acrylamide up to 4000 µg/kg may result in the consumption of 1000 µg of acrylamide in a single serving, with some people consuming two to three such servings per week; (c) a comparison of acrylamide content of potato chips (British crisps) with French fries on a dry weight basis indicates that roasted potatoes may contain >10000 µg of acrylamide/kg, exceeding that of potato chips (~500 µg/kg); (d) the high content of reducing sugars is primarily a consequence of the storage of fresh potatoes at 4 °C; and (e) to lessen acrylamide formation, the temperature of the frying oil should be ~170–175 °C.

Vivanti et al. (*6*) measured concentrations of acrylamide precursors asparagine, fructose, glucose, and sucrose in 9 potato varieties sold at retail in Italy and in 22 varieties sold in the United States (**Figure 8C**). Asparagine content ranged from 1.17 mmol/kg of fw for the Agata potatoes to 57.7 mmol/kg of fw for Russet potatoes, a 49.3-fold variation from the lowest to highest value. The levels of fructose ranged from 1.73 (Fingerling Ozette) to 33.6 (Red variety), a 19.3-fold variation. For glucose, the levels ranged from 1.11 (Jelli) to 34.73 (Yukon Gold B), a 31.3-fold variation. The values for sucrose ranged from 1.16 (Fingerling Ozette) to 40.6 (Marabel), a 35-fold variation. Such variation in free asparagine as well as free fructose, glucose, and sucrose contents of both Italian and American potatoes suggests that consumers, restaurants, and processors can select commercial potatoes with low levels of acrylamide precursors for baking or frying.

A related study found up to an 80-fold variation in reducing sugar content in commercial Irish potatoes (*28*). Initial reducing sugar, but not asparagine levels, correlated with acrylamide content of the French-fried potatoes. The final color of the fried potato measured with a HunterLab color meter correlated well with acrylamide concentrations, indicating that this parameter could serve as a convenient index for acrylamide content.

Acrylamide Precursors in Different Potato Cultivars. Acrylamide formation in 74 different potato cultivars correlated with their contents of fructose and glucose (*81*). Asparagine had less effect than reducing sugars, presumably because its content among the cultivars did not vary widely. Related studies showed that (a) acrylamide levels were highly correlated with both glucose and fructose contents of potato tubers (*82*); (b) acrylamide concentrations of French fries can be minimized by using potatoes with low amounts of sugars (fructose, glucose, sucrose) and to a lesser extent low amounts of asparagine (*72*); (c) acrylamide content in five potato varieties were significantly
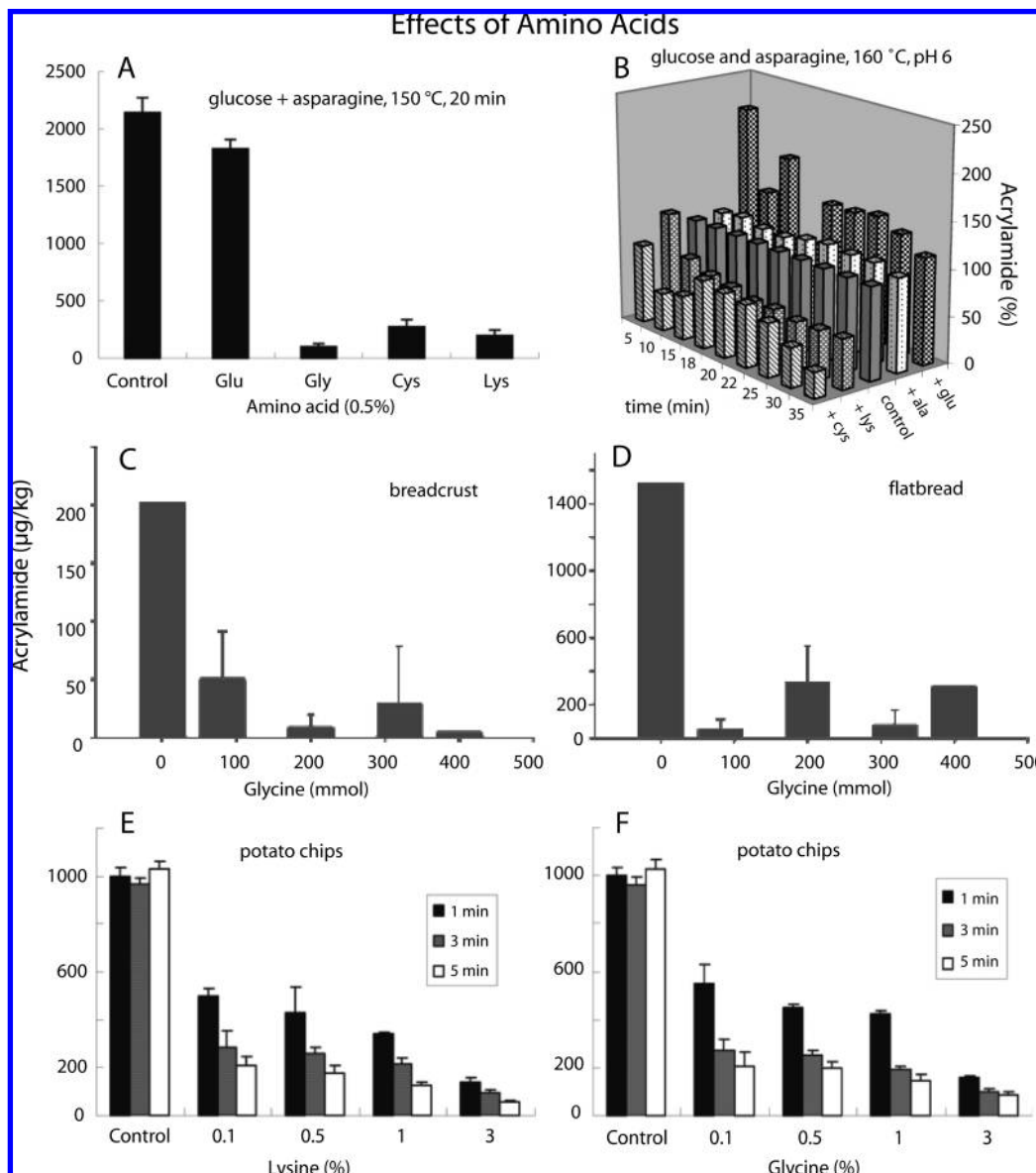
Figure 7. (**A**) Effects of amino acids on reduction of acrylamide in aqueous model systems. Amino acids were added at 0.5% to each aqueous solution containing 50 mM glucose and 50 mM asparagine. The mixtures were then heated in sealed glass tubes at 150 °C for 20 min. Cys, cysteine; Glu, glutamic acid; Gly, glycine; Lys, lysine. Adapted from ref *119*. (**B**) Effect of amino acids on the AA content (%) formed in an equimolar asparagine−glucose model system (control, 0.01 M, pH 6) heated at 160 °C. Adapted from ref *120*. (**C**) Effects of glycine on acrylamide in fried potato chips. Adapted from ref *119*. (**D**) Effects of glycine on acrylamide in fried potato chips. Adapted from ref *119*. (**E**) Effect of addition of glycine on the amount of acrylamide in bread crusts. Bars designate standard deviation and different letters significant differences. Adapted from ref *279*. (**F**) Effect of addition of glycine on the amount of acrylamide in flat breads. Bars designate standard deviation and different letters significant differences. Adapted from ref *279*.

influenced by reducing sugars rather than by asparagine (*83*); (d) both asparagine and reducing sugars increased concentrations of acrylamide in heated potato slurries (*84*); (e) asparagine levels increased during storage of Swedish potatoes (*73*), suggesting that the choice of potato clones with low asparagine content might minimize risk that the amino acid will increase during long-term storage; (f) in contrast, the asparagine content of the Japanese Toyoshiro potato tubers did not change during cold storage (*74*); (g) glucose, fructose, sucrose, and asparagine contents in potato tubers harvested in the United States increased during storage at 2 °C; glucose and fructose (but not sucrose and asparagine) levels correlated with acrylamide formation (*70*); and (h) cooling of American potatoes to <10 °C caused an increase in reducing sugars and a consequent increase in acrylamide amounts of fried potatoes, suggesting that the sugars determines the extent of acrylamide formation (*51*).

The cited studies again reinforce the idea that (a) a measurement of acrylamide precursors, especially reducing sugars, of potato varieties at a specific time may not always reflect levels present at earlier or later time periods; (b) to reduce cold-storage-induced sugar levels, potatoes should be reconditioned after storage; (c) postharvest handling of potatoes should be standardized to minimize the formation of reducing sugars; (d) plant scientists are challenged to develop potato cultivars that resist forming additional reducing sugars during cold storage; (e) to serve as a guide, the content of reducing sugars could be determined immediately before home and commercial processing of the potatoes.

Because labeling potatoes sold at retail may benefit consumers, we agree with the recommendation (*6, 79*) that potatoes should be labeled for reducing sugar content to minimize the use of cultivars with high reducing sugar content for high-heat
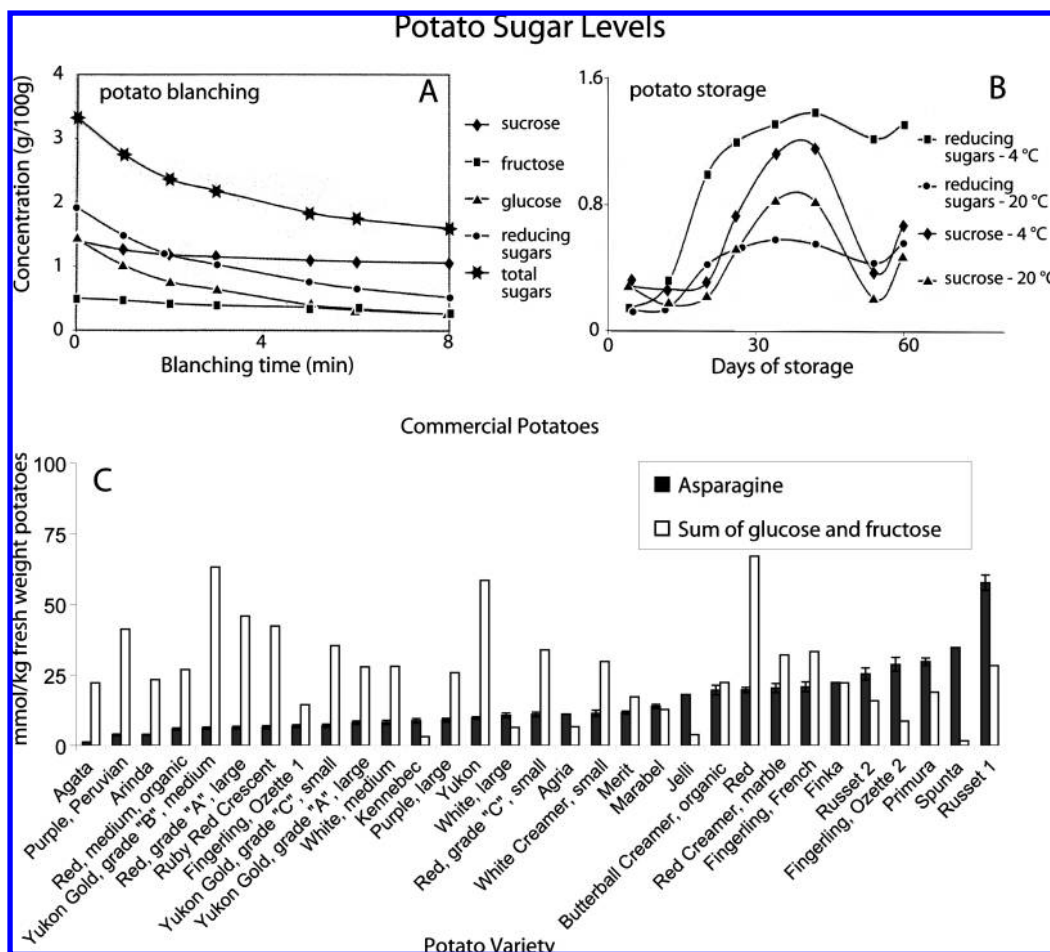
Figure 8. (**A**) Reduction in various sugar fractions with increasing blanching time of raw potato chips. Adapted from ref *92*. (**B**) Reducing sugar and sucrose content of Golden Delight potatoes stored at 20 or 4 °C. Adapted from ref *92*. (**C**) Relationship between increasing levels of asparagine in 31 potato samples and the sum of glucose and fructose. Adapted from ref *6*.

cooking. Such labeling may be facilitated by use of an inexpensive instrument that can rapidly measure glucose and fructose concentrations of the whole potato tubers, analogous to the use of such instruments to measure plasma sugar levels of diabetics (*85, 86*).

Effect of Moisture Content. Water plays a complex role in acrylamide formation and elimination, as illustrated by the following observations (see **Figure 12A**): (a) at low moisture levels, the activation energy for acrylamide formation in a potato model was larger (required more heat) than the corresponding activation energy for browning (*87*); (b) another study with a potato model showed that acrylamide formation during high-heat processing increased with higher water activities, whereas browning was greatest at intermediate water activities; at very high moisture levels, both the rate of browning and acrylamide formation decreased (*88*); (c) both acrylamide levels and browning in the crust of white bread increased with the crust temperature and with diminishing moisture content during oven baking; steam in the later stages of cooking reduced acrylamide formation while maintaining a desirable level of browning (*50*); (d) acrylamide formation during roasting of almonds was inversely related to the moisture content of the raw almonds (*89*); and (e) the rate constant for acrylamide formation in a model asparagine/glucose system varied only slightly with initial water activity, whereas the rate of acrylamide elimination was at a minimum at a water activity of 0.82, the same activity at which the Maillard reaction rate constant was greatest (*90*). These results indicate that the formation and elimination of

Maillard products and of acrylamide may be influenced differently by the water activity. By controlling moisture, it may be possible to uncouple these concurrent reactions. Desirable browning might be achieved without a commensurate increase in acrylamide levels.

Effect of Frying Conditions. The graphs in **Figure 9** visually depict the influence of several parameters on acrylamide levels of fried potatoes. Commercial White-Rose potatoes fried at 165 °C for 4 min at atmospheric conditions contained 5021 μg/kg acrylamide; Atlantic potatoes, 646 μg/kg; and Shepody potatoes, 466 μg/kg (*91*). The same study showed that vacuum frying at 118 °C resulted in a 94% reduction in acrylamide content of the chips compared to frying under normal conditions at 165 °C. Acrylamide concentrations of 66 potato samples fried at 180 °C for 3.5 min ranged from 50 to 1800 μg/kg (*72*). These results showed that significant reductions in acrylamide content can be achieved by using cultivars that generated low acrylamide levels during frying. Amounts of acrylamide formed correlated with reducing sugar and to a lesser extent with asparagine levels of the raw potatoes.

In a comprehensive study, May et al. (*92*) evaluated conditions that mitigate the formation of acrylamide in deep-fried potato products prepared in Australia. They found that (a) the rate of acrylamide formation as a function of temperature in the range from 140 to 180 °C increased linearly with an inflection point at ∼165 °C; (b) hot water blanching of raw potato chips for various times (1−8 min) at 95 °C resulted in an exponential decrease in reducing sugars, total sugar, and
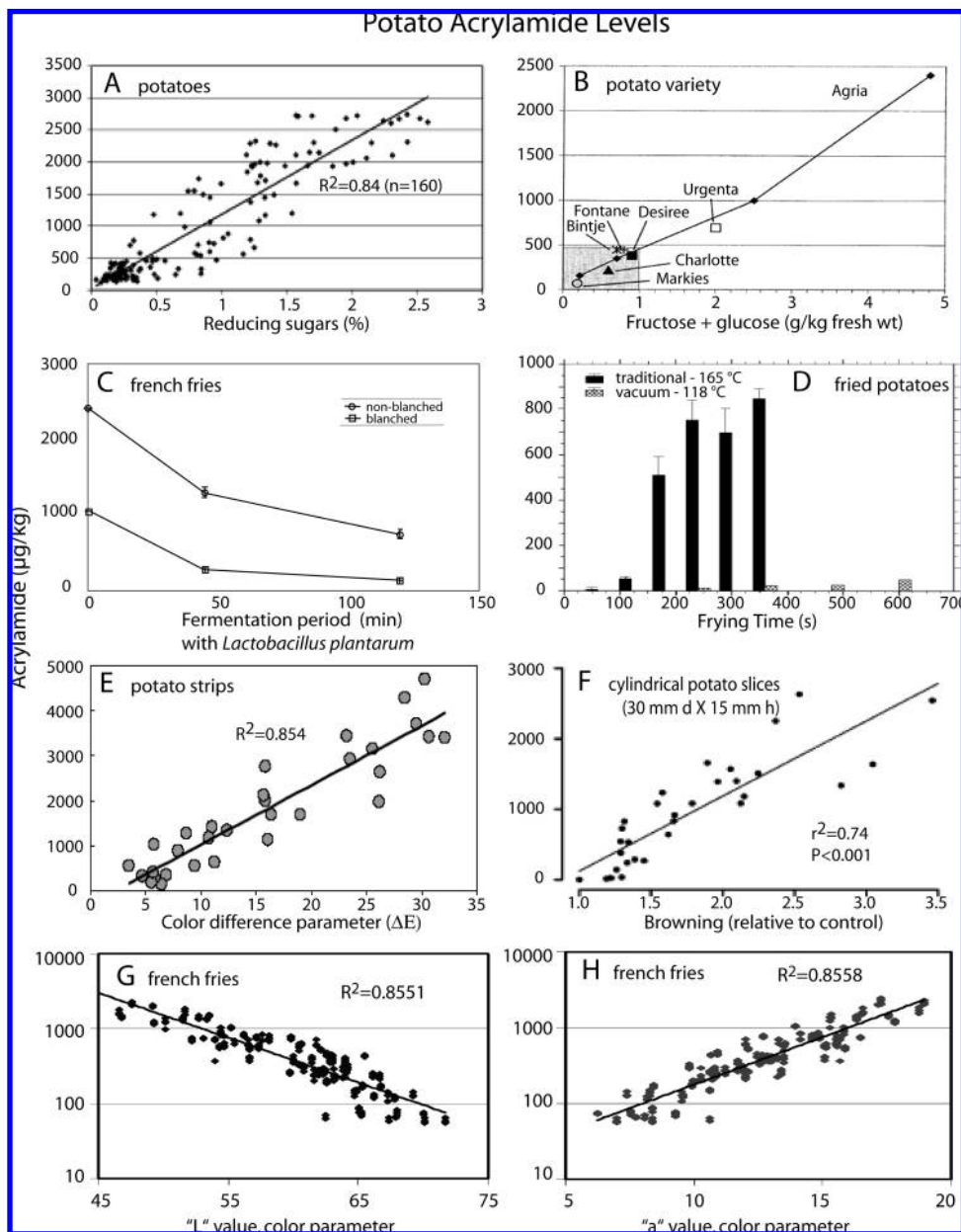
Figure 9. (**A**) Acrylamide as a function of the reducing sugars in potato tubers. Adapted from ref *93*. (**B**) Acrylamide contents in crispy Rösti depending on the content of reducing sugar in the potato. Gray area: under conditions minimizing acrylamide formation, potato containing up to 1 g/kg reducing sugar enables preparing Rösti of optimum quality with <500 μg/kg acrylamide. Adapted from ref *78*. (**C**) Reduction of acrylamide formation in French fries as a function of time of fermenting blanched and nonblanched potato rods with *Lactobacillus plantarum* NC8 [109 colony-forming units (CFU)/mL] before deep-frying. Bars show standard deviation of duplicate experiments. Adapted from ref *104*. (**D**) Effect of frying time on the acrylamide content of Atlantic variety potatoes fried in a traditional deep-fat fryer (165 °C) and a vacuum fryer (118 °C). Adapted from ref *91*. (**E**) Acrylamide content versus color difference parameter ΔE for potato strips fried at 150, 170, and 190 °C for all pretreatments tested. Adapted from ref *103*. (**F**) Correlation of acrylamide content with surface browning (expressed as the ratio of average pixel intensity of the sample image before frying to average pixel intensity after frying) in cylindrical slices of 30 mm diameter and 15 mm height [surface-to-volume ratio (SVR) 0.27 mm^{-1}] (cv. Bintje). *L* value measures the white−black component of surface color and *a* value, the degree of redness. Adapted from ref *76*. (**G**, **H**) Correlation between *L* and *a* color values and acrylamide levels in deep-fried French fries cooked for 0−10 min in corn oil at 150−190 °C. Adapted from ref *51*.

glucose levels (**Figure 8A**); at equilibrium the decrease in reducing sugar content ranged from 51 to 62% of original levels, with the reduction in small-sized chips averaging 35% and that in large-sized chips, 60%; (c) blanched and shallow-fried chips prepared at 180 °C contained 406% more acrylamide than did their blanched/deep-fried counterparts prepared at 190 °C; (d) unblanched shallow 180 °C fried chips contained 667% more acrylamide than did their blanched deep-fried counterparts; and (e) potatoes stored for up to 60 days at 4 °C contained higher sugar levels than those stored at 20 °C (**Figure 8B**). The rate

of accumulation of reducing sugars during storage differed among potato varieties that were evaluated. The authors conclude that the temperature of frying had a greater influence on acrylamide formation at low frying temperatures (>160 °C), that time of frying was more influential at higher temperatures (<170 °C), and that shallow-frying induced significant increases in acrylamide levels compared to deep-frying. The shallow-versus deep-frying results are significant and merit further study.

For potatoes grown in Belgium (*93*) it was observed that (a) storage at 4 °C enhanced acrylamide formation in French fries
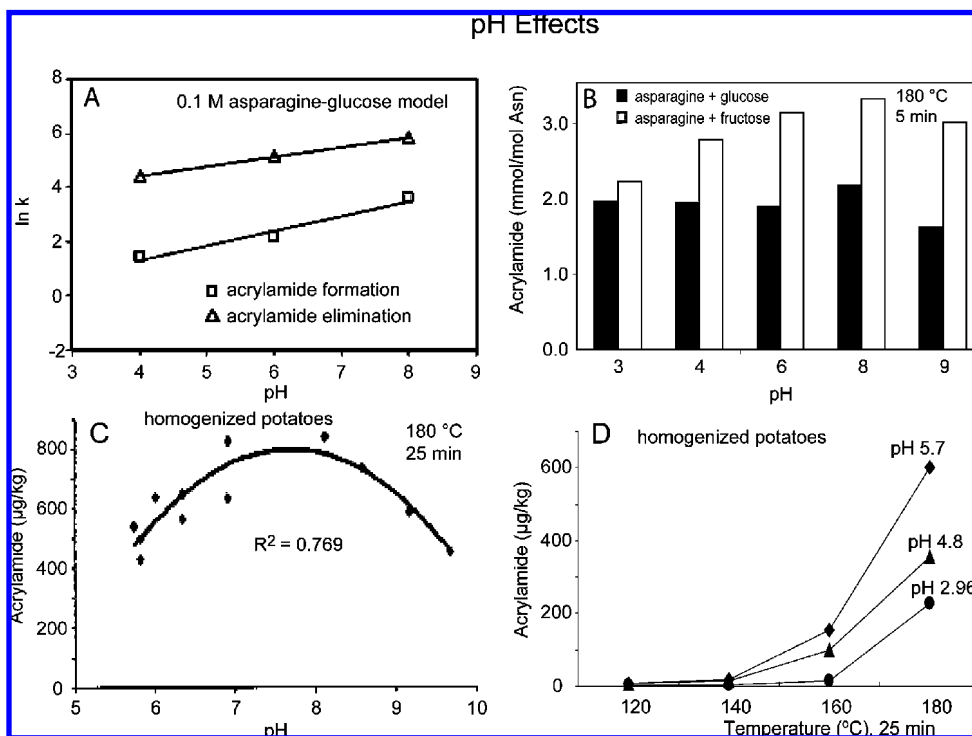
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Figure 10. (**A**) Relationship between pH and ln *k* for acrylamide formation (□) and elimination (△) in an equimolar asparagine−glucose (0.1 M) in phosphate buffer. Adapted from ref *105*. (**B**) Formation of acrylamide in binary mixtures of asparagine and glucose (black bars) or fructose (white bars) as a function of pH (180 °C, 5 min, 20 μL of water). Adapted from ref *37*. (**C**) Effects of pH on the content of acrylamide (in μg/kg) in homogenized potato heated in an oven. Heating was carried out at 180 °C for 25 min. Adapted from ref *106*. (**D**) Effect of pH on the content of acrylamide (in μg/kg) in homogenized potatoes heated for 25 min in an oven at different temperatures. The pH of the original sample was 5.72; acidification was achieved by the addition of HCl. Adapted from ref *106*.

compared to storage at 8 °C; (b) significant reduction in acrylamide content occurred following reconditioning of the cold-stored potatoes at 15 °C for 3 weeks; (c) changes in acrylamide amounts could be explained by storage-induced changes in reducing sugar levels of the potatoes ($R^2 = 0.84$; *n* = 160). The cited observations suggest that cold storage, known to increase the sugar content of potatoes, enhances acrylamide levels during frying and that reconditioning of potatoes at 15 °C before frying can be used to reduce sugar content and, consequently, acrylamide formation.

Because not all potatoes are the same, the cited study results reinforce the idea that selecting potato cultivars with low reducing sugar content can result in fries with low acrylamide content and that blanching soaking in hot water seems to be a simple process that can significantly reduce acrylamide concentrations of fried potatoes. Temperature of heating had a greater impact than time in the formation of acrylamide during the preparation of low-fat potato snacks (*77*).

Effect of Oil Degradation. Although oxidized lipids can serve as precursors of acrylamide (*42, 94*), no significant differences were observed in acrylamide formation in French fries that could be ascribed to oxidation or hydrolysis of the oils used in the frying experiments (*95*). Oxidation of lipids during potato frying did not result in enhanced acrylamide formation (*96*). Because of enhanced heat transfer, palm oil induced the formation of higher amounts of acrylamide than did other frying oils (*97, 98*). In contrast to glycoalkaloids (*99*), acrylamide did not leach into oil used to fry potatoes (*100, 101*).

Blanching and Soaking in Acid Solution. **Figure 8A** shows that blanching of potatoes results in significant reduction of reducing sugar levels. Related studies showed that soaking of potato crisps in acetic acid solution for 60 min at 20 °C prior to frying resulted in a 90% decrease in acrylamide content (*102*).

The pretreatment presumably extracted free amino acids and sugars that participated in acrylamide formation. Additional studies showed that acetic acid was more effective than citric acid solutions and that soaking in 1% sodium hydroxide also resulted in reduced acrylamide content of the crisps. Furthermore, postdrying of the crisps in a hot oven at 105 °C for 30−120 min also contributed to reductions in acrylamide levels. The possible impact of soaking on the nutritional quality of the crisps is not known.

Pedreschi et al. (*103*) observed that (a) immersion of potato strips in distilled water and in citric acid solution decreased acrylamide formation after frying; (b) long-time blanching treatments (50 °C for 80 min or 70 °C for 45 min) resulted in the lowest levels of acrylamide formation; (c) blanching removed more glucose and asparagine from the potatoes than did water immersion; (d) acrylamide formation diminished significantly with decreases in frying temperature from 190 to 150 °C for all pretreatments evaluated; and (e) there was a linear correlation between a color parameter and acrylamide levels of the French fries. On the basis of similar correlations between color values and acrylamide levels in French fries that have been deep-fried for 0−10 min in corn oil, Jackson and Al-Taheri (*51*) conclude that the degree of surface browning governs the final acrylamide content of French fries. The intensity of surface browning therefore appears to be a good marker for estimating acrylamide formation in French Fries during frying (see **Figure 9E−H**).

Lactic Acid Fermentation. Acrylamide formation during the production of French fries can be lowered by 48−71% by lactic acid fermentation of potato rods before deep-frying and by 79−94% by blanching the potatoes followed by lactic acid fermentation and deep-frying (*104*). The mechanism of this beneficial effect involves the conversion of reducing sugars by
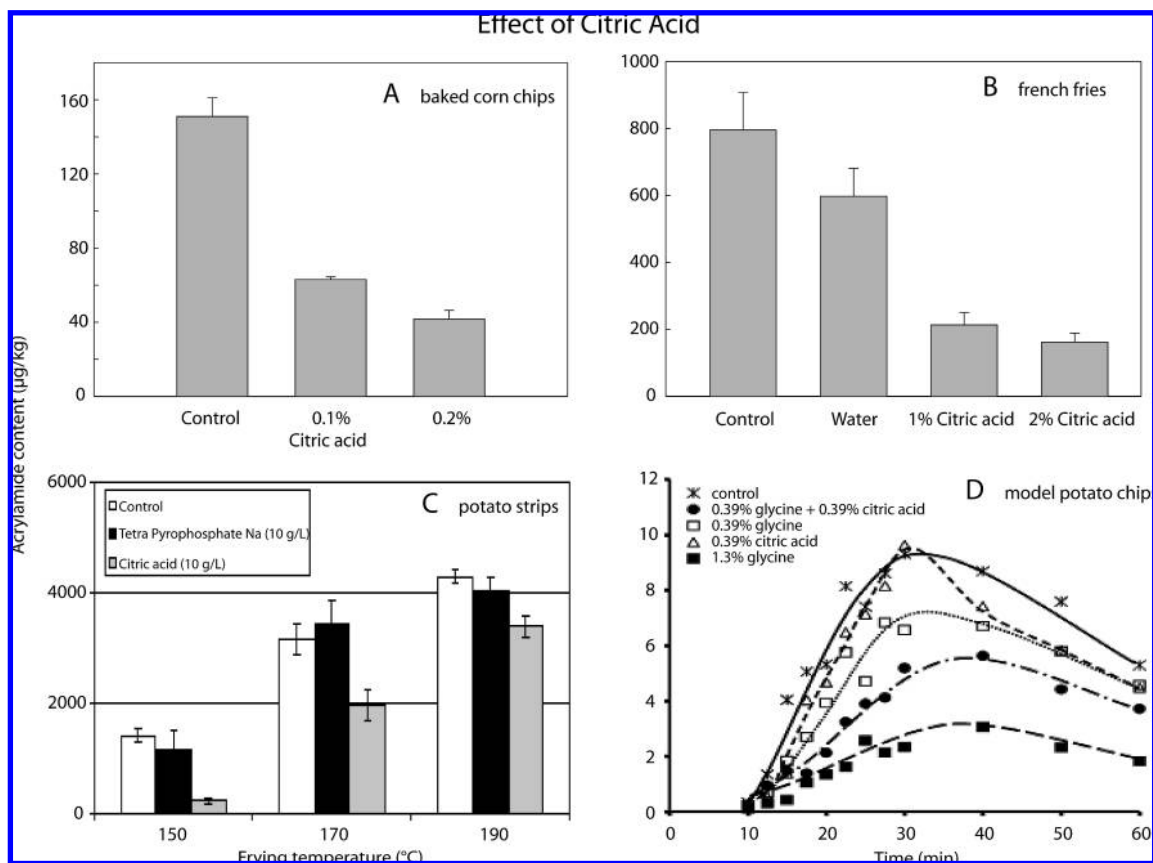
Figure 11. (**A**) Acrylamide formation in baked corn chips treated with 0, 0.1, and 0.2% citric acid. Adapted from ref *280*. (**B**) Acrylamide formation in French fries prepared after dipping in 0, 1, and 2% citric acid solution. Adapted from ref *280*. (**C**) Acrylamide content of control and potato strips dipped in sodium pyrophosphate and citric acid solutions of 10 g/L for 60 min after being fried at 150, 170, and 190 °C. Control corresponds to potato strips dipped in distilled water for 60 min. Adapted from ref *103*. (**D**) Formation of acrylamide in model potato cakes (set 1) cooked at 180 °C and formulated with the addition of glycine and/or citric acid. Adapted from ref *108*.

the *Lactobacillus plantarum* NC8 bacteria to lactic acid, which is accompanied by lowering the pH from 5.70 to ∼4.0 in the food matrix. Both acrylamide amounts and brown colors of French fries were reduced compared to fries prepared without fermentation.

Protective Effect by Acid pH, Acidulants, and Other Additives. The graphs in **Figures 10**, **11**, and **12** highlight reported studies on the impact of acid pH and of acids on acrylamide levels of potato products. The internal pH of a food can play a major role in governing acrylamide formation, as indicated by an assessment of the impact of pH on the kinetics of acrylamide formation and elimination reactions in a model asparagine/ glucose system and in a potato matrix (*105*). Acrylamide formation/elimination in phosphate and citrate buffers at dif- ferent pH values as a function of time and temperature showed that (a) maximum acrylamide levels are achieved through increasing temperature for shorter heating times; (b) at temper- atures <160 °C, acrylamide content decreased after prolonged heating, with acrylamide formation increasing at the first stage of heating, followed by elimination (destruction) at later stages of heating at higher temperatures (180−200 °C); (c) temperature dependence of the reaction rate constants increases with increasing acidity; and (d) for both formation and elimination of acrylamide, the reaction rate constant at 160 °C decreased 10-fold with decreasing pH from 8 to 4.

Studies by Rydberg et al. (*106*) showed that (a) reduction by acidification of the internal pH of the potatoes from 5.72 to 2.96 resulted in a ∼70% decrease; (b) added citric acid induced a concentration-dependent decrease up to ∼50% of the original level; and (c) in the pH range between 6 and 10, acrylamide

formation increased up to about pH 8, then decreased (see **Figure 10C,D**).

The following three acids induced significant reductions of acrylamide levels in French fries (% of control) (*107*): phos- phoric, 25; fumaric, 28; and tartaric, 29. The following acidulants (preservatives) also induced decreases in acrylamide content of the fries: benzoic, propionic, and sorbic acids. Citric acid and glycine also mitigated acrylamide formation in a potato model system (*108*).

These results indicate that increased acidity below pH 6 may be used to decrease acrylamide formation in potatoes and possibly other foods. It is also likely that the beneficial effects of low pH result not only from protonation of the reactive free α-NH_2 group of asparagine to the nonreactive α-NH_3^+ form but also from partial acid-catalyzed hydrolysis of asparagine to aspartic acid and of acrylamide to acrylic acid. However, low pH may adversely affect the taste of food (*15*). Also, as discussed before, if conditions are such that they lead to the hydrolysis of sucrose to glucose and fructose, this could have a positive effect on acrylamide formation. These aspects merit further study.

Protective Effect of Added Amino Acids. Previously, we have derived equations that were found to govern the pH dependence of the second-order addition reaction rates between of NH_2- and SH-containing amino acids and peptides to the double bonds of acrylamide and related conjugated vinyl compounds (*109–118*). The mathematical analysis makes it possible to optimize the pH of the reaction of various amino acids and peptides with known p*K* values and acrylamide, as illustrated in the Appendix.

Figure 7E,F shows that adding free amino acids (cysteine, glycine, lysine) to potatoes prior to processing results in reduced
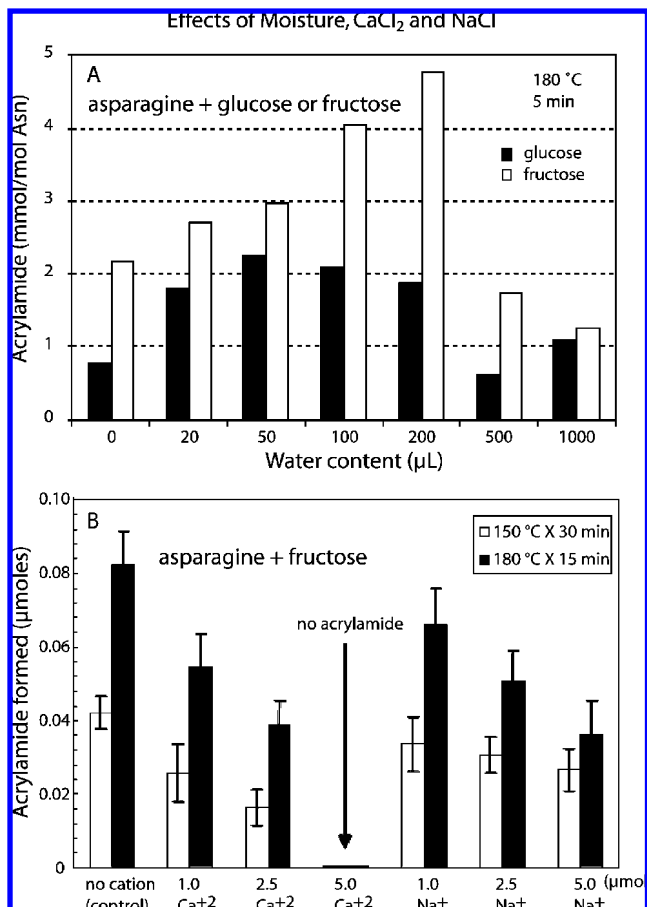
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Figure 12. (**A**) Formation of acrylamide in binary mixtures of asparagine and glucose (black bars) or fructose (white bars) as a function of moisture (180 °C, 5 min). Adapted from ref *37*. (**B**) Amounts of acrylamide formed (μmol) from asparagine (5 μmol) and fructose (5 μmol) in 100 μL of water heated in a sealed glass tube, as influenced by the presence of Ca^{2+} and Na^{+} in the reaction mixture. Adapted from ref *126*.

acrylamide levels in chips. Rydberg and colleagues (*106*) evaluated the influence of processing parameters and additives on acrylamide content of homogenized potatoes heated in an oven at 180 °C for 25 min (**Figure 10C,D**). Addition of non-asparagine amino acids reduced acrylamide formation markedly, probably due to competitive consumption of precursors and/or increased elimination/degradation. Addition of 140 mmol/kg of glutamine induced a 70% decrease of acrylamide levels compared to heated controls. The corresponding values for other amino acid were as follows: alanine, 50%; 4-aminobutyric acid, 86%; lysine, 88%; glycine, 91%. By contrast, addition of asparagine induced a 290% increase of acrylamide. The corresponding increases for fructose at 35 mmol/kg and 240 mmol/kg were 460 and 320% respectively, and those for glucose were 160 and 41%, respectively. We do not know why the higher amounts of the two reducing sugars induced lower increases in acrylamide levels. These authors (*106*) also discovered that addition of cod meat to grated potatoes resulted in a 70% decrease in acrylamide levels, suggesting that the fish matrix protected against acrylamide formation in fried potato patties. They state: "This may reflect a protective action of protein, for example, by elimination of acrylamide formed, perhaps via reaction with nucleophilic groups ($-$SH, $-$NH$_2$) on amino acid side chains".

Kim et al. (*119*) found that (a) added lysine, glycine, and cysteine significantly reduced acrylamide levels in an aqueous system; (b) added lysine and glycine were effective in inhibiting

the formation of acrylamide in wheat flour snacks; (c) adding 0.5% glycine to pellets reduced acrylamide concentrations by 70% in potato snacks; and (d) soaking potato slices in a 3% solution of glycine or lysine reduced acrylamide content of the potato chips fried for 1.5 min at 185 °C. These results suggest that soaking (dipping) of wheat flour dough and potato slices prior to processing in glycine or lysine solutions significantly reduces acrylamide content of the processed products.

A related study showed that the addition of cysteine or lysine to an asparagine/glucose model system heated between 140 and 200 °C significantly lowered acrylamide yield, whereas glutamine promoted acrylamide formation (*120*).

Glycine and lysine can exert their beneficial effects by competing with asparagine for the carbonyl group of the sugar moiety and/or form adducts with acrylamide after it is formed. In principle, the SH group of cysteine (or other thiols) can exert its beneficial effects in two ways: it can form an adduct with acrylamide as well as undergo heat-induced H_2S elimination to form dehydroalanine [CH_2=$CH(NH_2)COOH$]. The NH_2 group of asparagine can then competitively participate in addition reactions with the double bond of the dehydroalanine, as it does with acrylamide. Dehydroalanine can, in principle, also be formed by elimination of H_2O from serine (*121*). Evidently, free amino acids in foods can reduce as well as enhance acrylamide levels during processing and storage.

Protective Effects of Chickpea Proteins. Vattem and Shetty (*122*) investigated acrylamide formation in fried potato slices previously treated with phenolic antioxidants from cranberry and oregano or coated with a chickpea batter that forms a protein-rich snack widely consumed in India. Acrylamide content after deep-frying of untreated potato slices was 1490 μg/kg; for the cranberry-treated slices, 1030 μg/kg; for the oregano-treated slices, 1510 μg/kg; and for the chickpea batter treated slices, 580 μg/kg. On the basis of the cited observation that chickpea protein protected the slices against acrylamide formation, whereas the phenolic antioxidants did not, the authors suggest a nonoxidative model for acrylamide formation in the fried potato products. The protein content of the fried samples was inversely related to acrylamide levels. The protective effect of the chickpea proteins may be due to their known thermo-stability. The heat-stable proteins appear to function as a thermal barrier of the potato slices and/or to combine with some of the acrylamide as it is formed in the food matrix during frying. Alternatively, the protective effect may be due to the apparent inhibitory effect of proteins in general. These considerations raise the following questions:

• Because protein NH_2 and SH groups can react with acrylamide after it is formed, do processed high-protein foods (e.g., soy foods) contain less acrylamide than low-protein foods (e.g., cornbread)?

• Could replacement of egg and breadcrumb coatings with chickpea batter in the preparation of breaded chicken mentioned earlier result in reduced acrylamide levels?

• Does chickpea-based food widely consumed in India and the Mideast, for example, in falafel, protect against acrylamide formation?

Protective Effect of Soy Protein Hydrolysate. Adding soy protein hydrolysate prior to frying reduced acrylamide formation in hydrated potato flakes (*123*). The beneficial effect of the soy protein hydrolysate, like chickpea protein, presumably arises from the reaction of its peptide$-$NH$_2$ groups with acrylamide to form peptide$-$NH$-$CH$_2$CH$_2$CONH$_2$ derivatives. The potential of other protein hydrolysates to trap acrylamide in food merits further study.
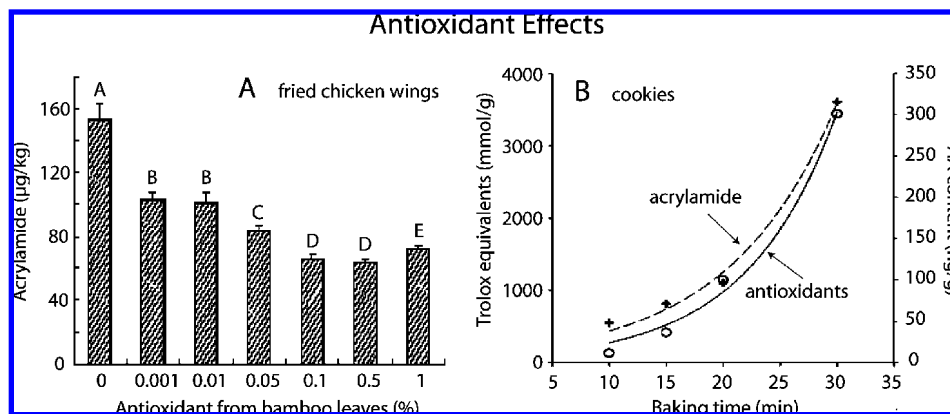
Figure 13. (**A**) Relationship between acrylamide levels and different conditions of antioxidant treatments from bamboo leaves in fried chicken wings (*n* = 6). Adapted from ref *281*. (**B**) Influence of the baking time on the concentration of acrylamide and on the antioxidants in cookie recipes containing 37% (w/w) sucrose: (○) acrylamide values; (+) antioxidant values; (solid line) regression curve for antioxidants; (broken line) regression curve for acrylamide content. Adapted from ref *282*.
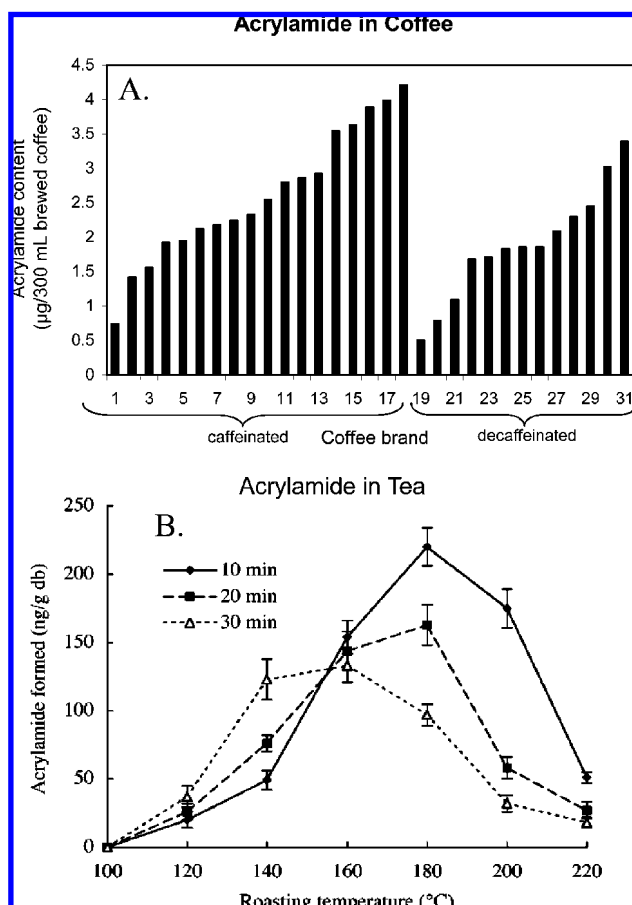

Figure 14. (**A**) Average level of acrylamide in 31 locally purchased ground coffees and the corresponding estimated level in 300 mL of brewed coffee. Adapted from ref *145*. (**B**) Effects of temperature and roasting time on acrylamide formation in roasted products. Tea leaves weighing 100 g were placed on an aluminum plate and roasted in a laboratory oven. Adapted from ref *150*.

Protective Effects of Metal Ions. **Figure 12B** illustrates the protective effects of $CaCl_2$ and NaCl against acrylamide formation in binary mixtures of asparagine with glucose or fructose. Related studies by Lindsay and Jang (*124*) showed that treating potato slices with a $CaCl_2$–phytate complex or with $FeCl_3$ could minimize acrylamide formation during frying. The authors suggest that ionic and electronic associations with asparagine suppress early-stage Maillard reactions. In comple-

mentary studies it was found that (a) 1% NaCl significantly reduced acrylamide formation in a heated asparagine/glucose model system (*125*); and (b) dipping potatoes into a $CaCl_2$ solution inhibited up to 95% of acrylamide formation during frying and that $CaCl_2$ completely and NaCl partly prevented acrylamide formation during heating of a fructose/asparagine solution (*126*). The preventive effect of Ca^{2+} ions may be due to the observed inhibition of the formation of the intermediate Schiff base that leads to acrylamide formation (*127*) (see **Figure 1**). Model studies showed that acrylamide elimination, possibly via polymerization, increased in the presence of table salt (*128*).

Previously, we found that changes of the ionic strength induced by positively charged Na^+ ions affect the rate of addition reactions of amino groups of amino acids to the double bonds of conjugated vinyl compounds such as acrylamide (*109, 111, 113, 116*). It is therefore also possible that changes in the ionic microenvironments near the potato strips contribute to the observed mitigating effects of positively charged metal ions (*129*).

Protective Effects of Antioxidants. **Figure 13** shows that added antioxidants resulted in reduced acrylamide levels in fried chicken wings and cookies. Related studies showed that addition of a proprietary antioxidative flavonoid spice mix (Flavomare) resulted in reduced acrylamide content of potato chips (*130*). Studies in China (*131, 132*) indicated that antioxidants present in bamboo leaves and other plants including tea reduced the formation of acrylamide in heated foods. Because tea contains high levels of antioxidative catechins and theaflavins (*133–135*), expectations are that the acrylamide content of roasted tea leaves should be low. However, tea, which is roasted during its preparation, had an average acrylamide concentration of 7.3 µg/kg (*74*), close to the FDA reported 7.8 µg/kg for coffee (*136*). No correlation was observed between acrylamide formation and antioxidants in a thermally processed model system of asparagine and glucose (*137*). Antioxidants present in cranberries and in oregano did not protect against acrylamide formation (*106*).

Antioxidants could exert their beneficial effects by abstracting reactive free electrons from free radical intermediates postulated to be formed in the Maillard reaction (*56, 138*).

Protective Effect of Premicrowaving. In comparison to controls, microwave precooking of potato strips prior to frying resulted in reduced acrylamide concentrations of 36, 41, and 60% for frying at 150, 170, and 190 °C, respectively (*139*). Ionizing radiation used to destroy pathogenic bacteria in food

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destroyed acrylamide in water but not in potato chips (*140*).

Acrylamide—Potato Glycoalkaloid—Polyphenolic Relationships. Glycoalkaloid levels of French fries were significantly reduced during peeling and blanching of potatoes, conditions that have also been found to minimize acrylamide amounts of the resulting products (*141*). Because glycoalkaloids can modify biological effects of acrylamide (*7, 99*), we do not know the consequences of the concurrent consumption of these ingredients. Both glycoalkaloids and phenolic compounds influence the flavor and taste of potatoes (*99, 138*), just as browning products do.

Acrylamide in Coffee, Tea, and Other Foods. *Coffee.* Figure **2** shows that the contribution of coffee to the total acrylamide content of the diet varies widely demographically, ranging from ∼8% for the United States, to 13% for The Netherlands, to ∼28% for Norwegian adults, and to ∼39% for Swedish adults. These results indicate that in many instances the amount of acrylamide that coffee contributes to the diet may be an important consideration in some populations.

Several studies have measured acrylamide in coffee (*142–144*). **Figure 14A** shows that trends in acrylamide content of different brands of caffeinated and decaffeinated coffees also vary widely, ranging from 0.5 to 4.21 μg/300 mL (*145*). The U.S. FDA reports that ground coffee contains 27−609 μg/ kg acrylamide (*146*). A joint report of the FAO/WHO reports that coffee powder contains 170−230 μg/kg acrylamide (*147*). Acrylamide concentrations following storage in the dark for 3−6 months at 10−12 °C did not change significantly for soluble coffee or for coffee substitutes, but decreased by 31% in coffee powder (*148*).

Andrzejewski et al. (*145*) found that levels ranged from 45 to 374 μg/kg in unbrewed coffee grounds, from 172 to 539 μg/ kg in instant coffee crystals, and from 6 to 16 μg/L in brewed coffees. Acrylamide remained stable in brewed coffee over 5 h on a hot plate and in sealed ground coffee stored at −40 °C over 8 months, whereas amounts decreased 40−65% in opened ground coffee stored at room temperature over 6 months. The storage history of the coffees may have contributed to the observed variations.

In related studies Lantz et al. (*149*) found that (a) acrylamide concentration in solid coffee reaches a peak during roasting, then decreased; (b) decreases in coffee during storage follow second-order kinetics, suggesting that they result from interaction of acrylamide with other coffee ingredients; (c) acrylamide in roasted coffee is largely extracted during brewing; and (d) a weak correlation (R (2) = 0.560) relates asparagine levels in green coffees to acrylamide content following roasting.

A review by Guenther et al. (*10*) states that there are currently no viable strategies for minimizing the acrylamide content in coffee, without adversely affecting the organoleptic qualities of the finished product. This observation is reinforced by the observation that increasing the degree of roasting of coffees resulted both in a desirable decrease in acrylamide levels and in an undesirable reduced radical scavenging capacity by concurrently formed melanoidin antioxidants (*144*).

Reductions in acrylamide levels during storage of cacao powder and coffee (*148*) may be the result of reactions of acrylamide with SH- and NH_2-containing amino acids, peptides, and proteins in these foods in the solid state. Other possibilities include hydrolysis, degradation, and polymerization of acrylamide during storage. Controlling the roasting temperature of green tea solids may result in low-acrylamide roasted tea beverages.

Table 5. Second-Order Rate Constants (k_2) for the Reaction of the S^- Group in $^-S−CH_2CH_2COO^-$ (Mercaptopropionic Acid) and the NH_2 Group in $NH_2−CH_2COO^-$ (Glycine) with Three Conjugated Vinyl Compounds at pH 8.1 and 30 °C

	k_2 (S^-) × 10^2, L/mol/s	k_2 (NH_2) × 10^5, L/mol/s	ratio of rates (S^-/NH_2)
acrylamide	0.46	2.60	178
acrylonitrile	2.70	20.4	132
methyl acrylate	11.0	76.0	145

Teas. **Figure 14B** illustrates effects of roasting temperature and time on acrylamide formation and destruction in teas. Specifically, Mizukami et al. (*150*) found that (a) roasting fresh tea leaves at 180 °C for 10 min resulted in the formation of significant amounts of acrylamide; (b) use of higher temperatures and longer heating times caused a decrease in acrylamide levels; (c) the asparagine content (0−0.6 mg/g, db) of 82 tea leaf samples correlated with acrylamide content (∼50−500 ng/g, db; r = 0.806); and (d) acrylamide content of roasted green tea infusions ranged from 4.8 to 41.2 ng/mL. These observations suggest that roasted tea has the potential to contribute significantly to the acrylamide burden of the diet.

However, except for acrylamide in roasted tea, for example, Hojicha brand, as well as in tea/grain (barley) combinations, for example, Mugicha and Hatomugicha brands, tea does not appear to be an appreciable source of acrylamide.

Curries. The acrylamide content of 30 Thai curries prepared in coconut milk ranged from 60 to 606 μg/kg of dry wt (*151*), a 10-fold variation from lowest to highest amounts. These results suggest that consumers can choose curries with low acrylamide content.

BIOAVAILABLITY AND MITIGATION OF TOXICITY

Bioavailability and Biomarkers. Bioavailability and biological activity of a food ingredient such as acrylamide depend on source and chemical and metabolic interactions. Here, we briefly examine how absorption, transport, and metabolism could affect the biological activity of dietary acrylamide in vivo.

Using a human intestinal model that measures the passage of acrylamide through the gastrointestinal epithelium of Caco-2 cells, it was observed that acrylamide was highly permeable, as evidenced by its ability to cross the cell monolayer in both directions via passive diffusion (*152*). In this model system, bioavailability was reduced in the presence of dietary proteins such as chicken egg albumin. Covalent modification of the SH and NH_2 groups of amino acids, peptides, and proteins by acrylamide in the alkaline pH environment of the distal jejunum, ileum, and colon would be expected to reduce the in vivo bioavailability of the acrylamide monomer. On the basis of these considerations, the authors suggest that a high-protein diet may reduce acrylamide uptake from the intestinal tract into the circulation.

A related study (*153*) also found that transport of acrylamide in the intestine is mediated primarily by passive processes, possibly combined with an energy- and pH-dependent active secretory component. Increasing acrylamide levels resulted in depletion of total cellular glutathione but not glutathione-*S*-transferase levels. Depletion of glutathione can favor cellular oxidative stress, which may be one possible mechanism of acrylamide genotoxicity. Significant amounts of dietary acrylamide consumed by pregnant women are transferred via blood through the placenta to the fetus (*154*). Breast milk was found to contain up to 18.8 μg/L acrylamide. Because water-soluble

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acrylamide can pass both placental and blood−brain barriers, the authors suggest that to protect fetuses, pregnant women should not consume high-acrylamide food. Acrylamide from poultry feed was carried over to the meat and eggs of laying hens (*155*).

Using hemoglobin adducts as biomarkers, Aureli et al. (*156*) compared the relative in vivo absorption by pigs of acrylamide present in drinking water and in heated food. The results indicated that absorption rates of acrylamide from water and animal feed were similar and that adduct levels were proportional to acrylamide intake (*35*).

Both acrylamide and its metabolite glycidamide are electrophilic compounds with a strong affinity for nucleophilic sites such as sulfhydryl and amino groups of amino acids, peptides, and proteins. The attraction between the electrophiles and nucleophiles results in the formation of adducts in vivo, in which acrylamide and glycidamide act as biological alkylating agents. Direct determination of hemoglobin adducts resulting from the reaction of acrylamide and glycidamide with terminal valine residues of hemoglobin in human plasma was found to be an important tool for risk assessment associated with human exposure to acrylamide. Although hemoglobin adduct formation is used to monitor the in vivo occupational and nonoccupational exposure to acrylamide from dermal contact, the diet, drinking water, and smoking (*157, 158*), its validity as a biomarker for acrylamide exposure is being debated (*159–161*).

Urinary *N*-acetyl-*S*-(propionamide)-L-cysteine and related metabolites have also been used to assess acrylamide exposure from smoke and from the diet (*162, 163*). However, the risk resulting from exposure to acrylamide derivatives and metabolites is largely unknown (*164–168*). There is a need to find out whether or not acrylamide and glycidamide adducts formed in vivo as well as acrylamide adducts formed in food are hazardous. Acrylamide also reacts with plant cells (*169*).

Bonding of CO_2 to N-terminal amino acids of the α- and β-hemoglobin chains in the lungs governs pH-dependent oxygen affinity (*170*). Previously we found that alkylation of NH_2 groups of amino acids with acrylamide and acrylonitrile lowers the p*K* values (basicities) of the adducts (*113, 171, 172*). These observations suggest that changes in the basic, hydrophilic/hydrophobic, and steric environments resulting from adduct formation of the N-terminal NH_2 group of the valine residue of hemoglobin (Hb−NH_2) by acrylamide and glycidamide to form Hb−NH−$CH_2CH_2CONH_2$ and Hb−NH−CH(OH)CH_2CONH_2, respectively, could potentially prevent CO_2 from covalently bonding to the amino termini of the hemoglobin adducts. This aspect merits study.

Chemoprevention of Toxicity by Dietary Ingredients. The following examples indicate that it may be possible to reduce adverse effects of acrylamide by chemoprevention: (a) The garlic ingredient diallyl sulfide, known to inhibit the liver enzyme cytochrome P450 2E1, decreased activation of acrylamide to the highly genotoxic glycidamide (*173*); (b) tea polyphenols, grape-derived resveratrol, and garlic-derived diallyl trisulfide decreased hemoglobin adduct formation in mice (*67, 174*); (c) a ginseng extract protected rats against toxic manifestation induced by acrylamide (*175*); and (d) phenylethyl isothiocyanate derived from cruciferous plants protected rats against acrylamide-induced testicular toxicity and, to a lesser extent, neurotoxicity. However, chlorophyllin and dietary fiber did not exhibit any protective effects in rats (*176*). These findings suggest that some dietary ingredients may reduce the toxic potential of acrylamide in humans.

It is not known how the concurrent formation of other processing-induced and natural food ingredients affects the dietary significance of acrylamide. Future studies should address the following questions:

• Do biologically active browning products (*7, 56, 177*) and other bioactive food ingredients (*178*) affect the safety of acrylamide after consumption?

• Do low amounts of dietary acrylamide potentiate the carcinogenicity of other carcinogens?

• Does the protein in hamburger meat mitigate the adverse effects of acrylamide of concurrently consumed fries?

• Do concurrently consumed food-related toxicants and beneficial food components modulate the safety of acrylamide in the human diet?

As very little is known to what extent these interactions actually occur in complex food systems and in vivo, predictions of the safety of acrylamide in foods based on the extensively reported studies with pure acrylamide may not always be justified. It may be predicted that antioxidative and genotoxic Maillard and related products (*7, 179, 180*) and carcinogenic heterocyclic amines (*181*) may modulate (enhance or suppress) possible carcinogenic and other adverse effects of acrylamide. However, the situation may be even more complicated because naturally occurring food ingredients could also modulate the safety of dietary acrylamide. These include embryotoxic (*182, 183*) and cancer cell-inhibiting glycoalkaloids (*99, 184, 185*), glycosidase-inhibiting calystegine alkaloids (*186, 187*), potato phenolic compounds (*138*), biologically active enzyme inhibitors (*188*), and degradation products of vitamin C present in cereal and potato products (*189–191*). In addition, cross-linked amino acids (lysinoalanine) (*4, 192–195*), D-amino acids (*3, 196*), nonenzymatic and enzymatic browning products (*7, 56, 197*), imidazolines (*198*), phenolic degradation products (*199*), and soybean enzyme inhibitors and lectins (*200–202*) as well as other naturally occurring antioxidative, antimutagenic, and anticarcinogenic polyphenolic compounds (anthocyanins, catechins, theaflavins, flavonoids) present in other vegetables, fruits, teas, and dark rice brans (*133, 135, 203–208*) and the anticarcinogenic amino acid theanine present in teas (*135*) as well as pungent capsaicinoids and piperines present in peppers (*209–211*) may also affect the toxic manifestations of dietary acrylamide. A striking example is our recent finding that dietary tomatine, previously found to be embryotoxic in frog assays (*212*), was not only nontoxic to rainbow trout but actually protected the fish against dibenzopyrine (DBP)-induced liver and stomach tumors (*213*).

It is also worth noting that dehydroalanine residues formed on exposure of food proteins to alkaline pH and synthesized in vivo (*214–217*), aflatoxin B_1 (*218–220*), and the potent tetrachlorimide mutagen formed in poultry processing water (*221*) can, in principle, alkylate proteins and DNA by mechanisms similar to that proposed for acrylamide (*5*). Could anticarcinogenic phenolic compounds, theanine, or tomato glycoalkaloids protect against adverse effects of acrylamide and other dietary biological alkylating agents of DNA? It would be also worthwhile to find out whether several food-compatible compounds that have been reported to inhibit glycation of hemoglobin by glucose in vivo would inhibit acrylamide formation in food. These compounds include acetaldehyde (*222*), L-arginine and sperminidine (*223*), pyridoxamine (*224*), pyruvate (*225*), taurine (*226*), and urea (*227*).

RESEARCH NEEDS

Recent epidemiological reports that dietary acrylamide was linked to significant increases in the incidence of breast,

endometrial, and ovarian cancers in women (*228, 229*) reinforce the need to reduce the acrylamide content of the diet and to mitigate adverse in vivo effects after consumption. The results of extensive worldwide studies described in this review indicate that we may have reached a watershed in efforts to mitigate the adverse impact of dietary acrylamide on food safety and human health. The use of one or more of the 30 approaches listed in **Table 4** should enable the design of alternative food processes to minimize the formation and biological utilization of potentially toxic acrylamide while maintaining desirable nutritional and sensory attributes acceptable to consumers.

Ongoing studies that are relevant to the theme of this paper that may facilitate future progress include (a) development of improved extraction and analysis conditions for precursors and for acrylamide in food (*142, 230–233*) and in waters (*234, 235*); and (b) new observations on the biochemistry, metabolism, pharmacology, toxicology, and pathogenesis of acrylamide (*236–261*). The cited studies demonstrate the continuing interest in the potential adverse impact of acrylamide on food safety and human health.

This overview covers an area of food science of current importance to consumers, food and biomedical scientists, food manufacturers, and government regulatory agencies. We are also challenged to educate food processors, bakers, restaurant operators, and consumers about ways to modify culinary practices that will reduce the formation and increase elimination of acrylamide during commercial and home processing of different food categories.

Our assessment also shows the need for additional research designed to mitigate the dietary impact of acrylamide. A number of research needs related to the chemistry and biological effects of acrylamide have been mentioned in the text. The following additional suggested research approaches are designed to facilitate reducing acrylamide levels in processed food and minimizing the bioavailability of acrylamide in the human diet.

1. Devise improved methods to decrease the concentrations of acrylamide precursors in food while maintaining desirable nutritional and sensory properties.

• Develop databases of asparagine/glucose content of commercial foods.

• Select from available cultivars (e.g., potatoes, cereal grain, coffees) those that contain low levels of free asparagine for food use.

• Develop new low-asparagine and low-glucose cultivars by breeding and plant molecular biology techniques.

• Optimize hydrolysis of the amide group of asparagine in food to aspartic acid and ammonia by acids, bases, and asparaginases.

• Optimize effects of acids that transform the reactive α-NH$_2$ group of asparagine to the protonated uncreative α-NH$_3^+$ form.

• Modify the α-NH$_2$ group of asparagine by acylation, Schiff base formation, methylation, etc.

2. Transform and/or trap acrylamide after it is formed in food.

• Optimize acid-, base-, and enzyme-catalyzed hydrolysis of the amide group to acrylic acid and ammonia.

• Define relative effectiveness (kinetics) of naturally occurring amino acids and peptides to form acrylamide adducts during food processing.

• Define effectiveness of naturally occurring antioxidative compounds (plant anthocyanins, catechins, flavonoids, polyphenolic compounds) to prevent acrylamide formation during processing.

• Determine whether fried and roasted potatoes prepared from polyphenol-rich unpeeled potatoes contain less acrylamide than those prepared from peeled potatoes.

• Polymerize acrylamide in food to poly acrylamide prior to consumption.

3. Mitigate adverse manifestations of acrylamide after consumption.

• Define possible additive and synergistic carcinogenic effects of dietary acrylamide consumed at low levels and other dietary carcinogens (aflatoxin B$_1$, heterocyclic amines, *N*-nitroso compounds).

• Define effects of processing-induced food ingredients (browning products, fatty acid oxidation products) on the safety of acrylamide.

• Define impact of plant secondary metabolites (phenolic compounds, glycoalkaloids, pungent pepper compounds) on the safety of acrylamide.

• Define impact of nutrients (carbohydrates, free amino acids, proteins, fats, vitamins, minerals) and of malnutrition on the toxicity of acrylamide.
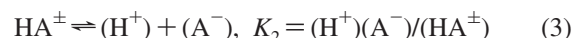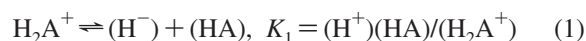
• Induce expression of genes coding for enzymes (glutathione-*S*-transferases, phase-2-detoxifying enzymes) that catalyze the metabolism and excretion of acrylamide and glycidamide (*165, 262, 263*).

• Suppress expression of genes coding for enzymes that catalyze the epoxidation of acrylamide to the more toxic glycidamide.

In conclusion, the main objective of this overview was to showcase efforts designed to reduce the acrylamide content of processed foods and to mitigate adverse manifestation of acrylamide after consumption. We anticipate that this effort will contribute to the improvement of food safety and human health.

APPENDIX: pH DEPENDENCE OF REACTION RATES OF AMINO ACIDS WITH ACRYLAMIDE

To facilitate the use of amino acids to reduce acrylamide levels in food, we offer the following derivation of the equation that describes the variation of the rate constants with pH for the reaction of amino acids with conjugated vinyl compounds such as acrylamide (*109–118, 236*). Note that the rates vary for different amino acids and increase rapidly as the pH approaches the p*K* of the amino group. The change in the reaction rate constant with pH in terms of the concentration of each of the amino acid species may be derived from the ionization constants of the amino acids. The following equations represent the equilibria of amino acids in solution:

$$\text{H}_2\text{A}^+ \rightleftharpoons (\text{H}^-) + (\text{HA}), \ \ K_1 = (\text{H}^+)(\text{HA})/(\text{H}_2\text{A}^+) \quad (1)$$

$$\text{HA} \rightleftharpoons \text{HA}^\pm, \ \ K_\text{D} = (\text{HA}^\pm)/(\text{HA}) \quad (2)$$

$$\text{HA}^\pm \rightleftharpoons (\text{H}^+) + (\text{A}^-), \ \ K_2 = (\text{H}^+)(\text{A}^-)/(\text{HA}^\pm) \quad (3)$$

H$_2$A$^+$ is the amino acid cation, HA is the neutral form, HA$^\pm$ is the zwitterions, and A$^-$ is the anion.

The following terms are defined as V_1 = velocity due to the reaction of acrylamide with HA, V_2 = velocity due to the reaction of acrylamide with A$^-$, k_2 = observed overall second-order rate constant, k_HA = second-order rate constant associated with species HA, k_{A^-} = second-order anion rate constant associated with species A$^-$, and (*B*) = concentration of acrylamide.

Because H$_2$A$^+$ = (H$^+$)(A$^-$)/$K_1K_2^-$, HA = (H$^+$)(A$^-$)/K_2K_D, and HA$^\pm$ = (H$^+$)(A$^-$)/K_2, the concentration of all unreacted amino acid species (AA)$_\text{T}$ equals

$$(AA)_T = (H_2A^+) + (HA) + (HA^\pm) + (A^-) = [(H^+)^2/K_1K_2 +$$
$$(H^+)/K_2K_D + (H^+)/K_2 + 1](A^-) =$$
$$\frac{[(H^+)^2K_D + K_1(1 + K_D)(H^+) + K_1K_2K_D]}{K_1K_2K_D}(A^-)$$

Solving for (A^-)

$$(A^-) = \frac{K_1K_2K_D(AA)_T}{K_1K_2K_D + K_1(1 + K_D)(H^+) + K_D(H^+)^2}$$

$$V_1 = k_{HA}(HA)(B); \quad V_2 = k_A - (A^-)(B)$$

$$V_T = V_1 + V_2 = -[k_{HA}(H^+) + k_A - K_2K_D](A^-)(B)/K_2K_D$$

Substituting for (A^-) and equating theoretical and experimental velocities

$$-\frac{[k_{HA}(H^+) + k_A - K_2K_D]K_1(AA)_T(B)}{[K_1K_2K_D + (H^+)K_1(1 + K_D) + K_D(H^+)^2]} = k_2(B)(AA)_T$$

$$k_2 = \frac{k_{HA}(H^+)k_1}{[K_1K_2K_D + (H^+)K_1(1 + K_D) + K_D(H^+)^2]} +$$
$$\frac{k_A - K_1K_2K_D}{[K_1K_2K_D + (H^+)K_1(1 + K_D) + K_D(H^+)^2]} \quad (4)$$

Equation 4 relates the observed second-order rate constant to the second-order rate constants of the two reactants in solution, the neutral amino acid HA and the amino acid anion A^-, the hydrogen ion concentration, and the three equilibrium constants of the amino acid.

Equation 4 may be simplified by making the following approximations: Because $K_D \sim 10^5$, $1 + K_D \approx K_D$, and because H^+ is small $(H^+)^2$ may be neglected and $(H^+)/K_D \rightarrow 0$. The first term drops out, resulting in the operative eq 5:

$$k_A - = k_2\left[1 + \frac{(H^+)}{K_2}\right] \quad (5)$$

Figure 15 shows that reaction rates of α-NH$_2$ groups of structurally different amino acids and peptides with acrylamide and related α,β-conjugated compounds are linear functions of the basicities (pK_2 values) of the NH$_2$ groups. On the basis of this observation, we may predict that the relative effectiveness of structurally different amino acids to trap acrylamide in food will depend both on the pH of the liquid medium and solid food and on the pK_2 values and structures of amino acids and peptides. Related studies show that dimethyl sulfoxide (DMSO) accelerates reaction rates of NH$_2$ groups of amino acids and peptides (*112*) and that SH-containing compounds are more reactive than analogous NH$_2$-containing ones (*115*) (**Table 5**). In principle, the α-NH$_2$ groups of glycine and valine, the ϵ-NH$_2$ group of lysine, NH$_2$ groups of nucleic acids, can form both mono- and disubstituted derivatives with acrylamide, as illustrated with glycine:
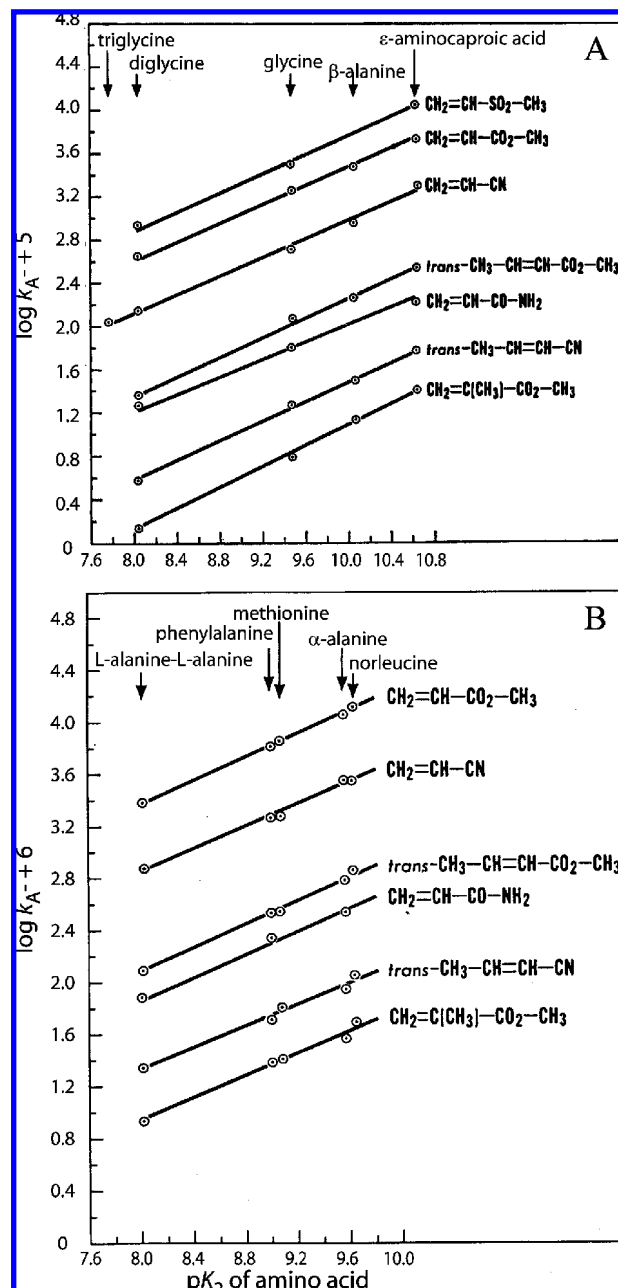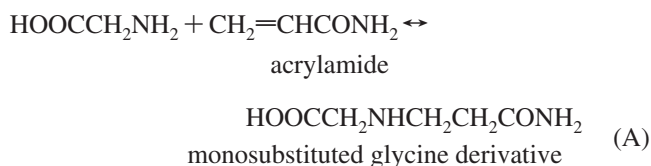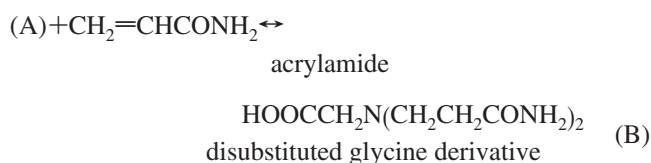
HOOCCH$_2$NH$_2$ + CH$_2$=CHCONH$_2$ $\leftrightarrow$
acrylamide

HOOCCH$_2$NHCH$_2$CH$_2$CONH$_2$ (A)
monosubstituted glycine derivative

Figure 15. Linear plots of log k_A- versus pK_2 values for the reaction of amino acids and peptides with acrylamide (CH$_2$=CH—CO—NH$_2$) and related conjugated compounds. Note that the rates for amino acids of structure NH$_2$(CH$_2$)$_n$COOH (i.e., glycine, n = 1, in **A**) are $\sim$10 times greater than those of structure NH$_2$(CHR)$_n$COOH (i.e., α-alanine, R = CH$_3$, n = 1, in **B**). Note that only the amino acid anion (NH$_2$CH$_2$COO$^-$) can react with acrylamide. The cation (NH$_3^+$CH$_2$COOH) and the zwitterion (NH$_3^+$CH$_2$COO$^-$) forms cannot. The order of reactivities of vinyl compounds is methyl vinyl sulfone (**A**) > methyl acrylate > acrylonitrile > *trans*-methyl crotonate > acrylamide > *trans*-crotonitrile > methyl (2-methyl) acrylate. Adapted from refs *109, 111*, and *113*.

(A) + CH$_2$=CHCONH$_2$ $\leftrightarrow$
acrylamide

HOOCCH$_2$N(CH$_2$CH$_2$CONH$_2$)$_2$ (B)
disubstituted glycine derivative

The SH and NH$_2$ functionalities of cysteine [(HS—CH$_2$CH-(NH$_2$)COOH] can theoretically form up to three acrylamide derivatives. Elsewhere, we also offer mathematical analyses of

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such pH-dependent competitive, consecutive reactions involving NH$_2$ and SH groups of amino acids that are applicable to acrylamide (*110, 115, 264*). Not surprisingly, the reactions we observed in vitro appear to parallel analogous transformations in vivo (*255*). Research continues in this important area (*283–295*).

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