SHUTTERSTOCK (ALL)

THE MAILLARD REACTION TURNS 100

It's the **CENTENNIAL OF A REACTION** that makes cooked food tasty but also produces worrisome molecules

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BAKED BREAD, roasted coffee, and grilled steak owe their enticing smell to a sequence of chemical reactions that was first reported 100 years ago by the French chemist Louis-Camille Maillard.

His 1912 paper took a first stab at explaining what happens when amino acids react with sugars at elevated temperatures, and in doing so, Maillard set the foundations of serious food science (*Compt. Rend.* **1912,** *154,* 66).

Although it is responsible for some of cooked foods' more delightful flavors as well as the brown color of bread crusts, soy sauce, and barbecued meat, the Maillard reaction also has a dark side: It can produce cancer-causing acrylamide and furans in food, particularly highly processed or burnt meals. Medical researchers have also discovered that the Maillard reaction takes place spontaneously in human tissue, and its products have been linked to a variety of diseases, including diabetes and cataracts.

"The Maillard is, by far, the most widely practiced chemical reaction in the world," said chemistry Nobel Prize winner Jean-Marie Lehn late last month in Nancy, France, some 20 miles from the village of Pont-à-Mousson, where Maillard was born. That's because the reaction takes place daily in households around the globe whenever food is cooked, Lehn told the group of 270 international scientists who had gathered on Maillard's home turf to honor the reaction's centennial and attend this year's International Maillard Reaction Society conference.

Prior to Maillard's paper in 1912, which described the reaction between reducing sugars and amino acids, "there wasn't much of what you could call flavor chemistry," said Alan Rocke, a historian at Case Western Reserve University. "There were lots of ideas and anecdotes, but no proper science."

Yet even with the simplest of reactants, Maillard chemistry was so complicated and produced so many products—hundreds of them—that the research world would largely ignore it until around the time of World War II, Rocke said. That's when the military became interested in producing on an industrial scale food that both was palatable and had a long shelf life. Because the Maillard reaction is responsible for the appealing aromas of freshly cooked food as well as some of the unwelcome ingredients in processed or long-stored food, scientists began to seriously study the reaction, Rocke explained.

THEN IN 1953, an African American chemist named John E. Hodge, who worked at the U.S. Department of Agriculture in Peoria, Ill., published a paper that established a mechanism for the Maillard reaction (*J. Agric. Food Chem.* **1953,** *1,* 928).

"Maillard discovered the reaction, but Hodge understood it," said Vincenzo Fogliano, a food chemist at the University of Naples, Federico II. In fact, because citations of Hodge's paper far outnumber those of Maillard's, there has been some discussion of renaming it the Maillard-Hodge reaction, Fogliano said. But that idea hasn't yet caught on.

According to Hodge's model, the Maillard reaction has three stages. First, the carbonyl group of a sugar reacts with an amino group on a protein or amino acid to produce water and an unstable glycosylamine. Then, the glycosylamine undergoes Amadori rearrangements to produce a series of aminoketose compounds. Last, a multitude of molecules, including some with flavor, aroma, and color, are created when the aminoketose compounds undergo a host of further rearrangements, conversions, additions, and polymerizations.

SECRET INGREDIENT The Maillard reaction creates many of the delicious colors and odors of cooked food.

The reaction forms thousands of compounds in food, said Thomas Hofmann, the chair of food chemistry and molecular sensory science at Technical University of Munich. And of those, only a small subset repeatedly contribute to the odor and flavor of cooked food, such as 2,3-butanedione in popcorn and grilled steak.

Over the past several decades, there's been a huge effort by food scientists to figure out how to influence the end products, Fogliano said. They've looked at various starting sugars and proteins as well as how different temperatures, pH levels, moisture levels, and other ingredients affect the creation of desired and undesired odor and flavor products. The idea, he added, is to figure out how to control the unruly Maillard process as it happens in food.

For example, Hofmann said, "it's primarily the amino acid that drives the odor quality, not the sugar." Glycine reactions produce beerlike odors, valine reactions produce characteristic rye-bread smells, and cysteine is the amino acid responsible for many meat and cracker scents, he said.

MAILLARD REACTIONS can also change the texture and consistency of food, said Thomas Henle, a food chemist at Dresden University of Technology. For example, the Maillard reaction is used to append sugars to the protein lactalbumin, which is then used to make yogurt more gelatinous. Meanwhile, adding sugar to a protein called β-lactoglobulin in processed cheese makes the product softer and creamier, he said.

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Maillard

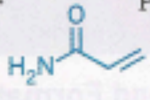
Sometimes a Maillard product that is appealing in some processed foods is undesirable in others. Case in point: 2-acetyl-1-pyrroline. This molecule gives crusty bread, popcorn, and basmati rice a desirable odor and flavor, but its presence in ultra-high-temperature pasteurized milk, because of the processing, results in an off-putting aftertaste that many consumers dislike, Hofmann says.

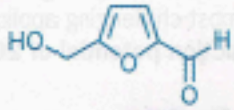
More notorious outcomes of the Maillard reaction in food are 5-hydroxymethylfurfural (HMF) and acrylamide, both potential carcinogens. Ten years ago, Stockholm University food chemists Margareta Törnqvist and Eden Tareke published a paper that sent shock waves through the food regulatory and science community: They showed that heavily processed food such as french fries, chips, and biscuits contained milligram levels of acrylamide (*J. Agric. Food Chem.*, DOI: 10.1021/jf020302f).

The discovery came after a sequence of unusual, coincidental events. A Swedish construction team using polyacrylamide to plug leaks in a tunnel became ill, and Törnqvist was asked to investigate the workers' exposure to acrylamide. But when she looked for healthy members of the public to use as controls, they too had unexpectedly high levels of acrylamide. At the same time, Tareke was studying acrylamide levels in wild animals and domesticated pets, and she found unexpectedly high levels of the compound in pets, she told C&EN. Because a main difference between wild and domesticated animals is their consumption of highly processed pet food, the researchers began to wonder whether the levels of acrylamide in humans are also attributable to consumption of highly processed food. Then they showed that processed food did in fact have substantial levels of the chemical.

Since 2002, food scientists and the food industry have devised a multitude of ways to reduce levels of acrylamide and other health-concerning molecules such as HMF in food. And according to Monica Anese, a food scientist at the University of Udine, in Italy, they have implemented some of the methods.

One of the most promising techniques for acrylamide removal, she said, is the preprocessing use of an enzyme called asparaginase, which can break down the amino acid asparagine. Acrylamide is produced when asparagine reacts with sugar, so removing the amino acid at the outset of processing helps reduce acrylamide levels in the final foodstuff. Another strategy is to lower cooking temperature, although this makes cooked food such as cookies and bread less brown—which consumers typically don't like, she said.


Acrylamide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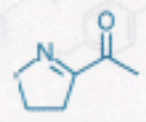
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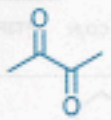
2,3-Butanedione

Although the past decade has witnessed an increase in concern about the possible long-term consequences of consuming unwanted Maillard products in processed food, medical researchers have been worried about the outcome of endogenous Maillard reactions in our own bodies since the 1960s. After all, we are chock-full of proteins and sugars, and the Maillard reaction can take place at lower temperature as well, albeit at much slower rates of reaction, said Vincent M. Monnier, a medical researcher at Case Western Reserve.

One reaction hot spot is the lens of the human eye, where Maillard-based chemistry is partly responsible for nuclear cataracts. In this prevalent form of the disease, the cataracts darken and need to be extracted, he said. Because lens cells don't regenerate over a lifetime and they have high levels of ascorbic acid, which can enhance Maillard reactions, "the lens is a trash can for human Maillard reactions," he added.

DIABETES IS ANOTHER major area of medical Maillard research. The increased levels of sugar in the bloodstream result in Maillard reactions that activate the body's inflammation response and contribute to many of the liver and cardiovascular complications of the disease, Monnier said.

In fact, the human body has several endogenous systems in place to remove these Maillard reaction products, said Paul Thornalley, a researcher at England's Warwick Medical School. Thornalley studies enzymes that our body produces to eliminate methylglyoxal, a common Maillard reaction product circulating in our bloodstream. Left unchecked, methylglyoxal wreaks all sorts of damage, including interfering with cell surface proteins needed to keep blood vessel cells attached to each other. Although the enzymes responsible for breaking down methylglyoxal work 99.7% of the time, some methylglyoxal still "slips under the fence and does damage, particularly in diabetics," he said.

After 100 years of studying the reaction, we've come to realize "there's really a Maillard paradox," Monnier said. "Cooking kills bacteria, increases shelf life, and creates attractive aromas." But these same processes can create harmful chemicals in food. And in our body, the reaction is linked with inflammation, diabetes, and cardiovascular disease, he adds.

Maillard himself probably would have been more fascinated with the modern medical applications of the reaction rather than the initial food ones, Rocke said. When Maillard discovered the reaction, the scientist was looking for ways to synthesize proteins in vitro, Rocke said. The odors and colors emerging from his lab bench probably directed him more toward food chemistry applications, "but he was really a biochemist at heart," Rocke said. ■