The Maillard reaction in food: Progress made, challenges ahead—Conference Report from the Eighth International Symposium on the Maillard Reaction

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The Eighth International Symposium on the Maillard reaction marked the 25th anniversary of the first symposium and saw a change in focus away from food processing aspects, towards health and nutrition. In the medical arena, research into aging and diabetes has an increasingly broad scope, including human health, disease and nutrition. Thus, the boundaries between food scientists and medical researchers are becoming increasingly blurred, and a common goal of establishing the physiology and fate of Maillard reaction products absorbed from the diet or generated in vivo has emerged. This review highlights some new directions in Maillard research of relevance to food scientists that emerged during the conference.

History

Over the past century, food scientists have played a critical role in unraveling the chemistry of the Maillard reaction (Baynes, Ames, Monnier, & Thorpe, 2005), setting the stage for those now focused on the reaction in biological systems. More recently, researchers have isolated and structurally characterised 25 Maillard reaction products (MRPs) from tissues in the body, with more being reported at an increasing rate in the scientific literature (Baynes & Thorpe, 2004). In the medical arena, attention has shifted from an original interest in aging and diabetes, to a broader scope including human health, disease and nutrition. Thus, the boundaries between food scientists and medical researchers are disappearing. This was an emerging theme at the Eighth International Symposium on the Maillard reaction held recently in South Carolina (Baynes et al., 2005).

The first Maillard symposium was held in Sweden in 1979 (Eriksson, 1981). The focus was very much on food chemistry—both beneficial and negative impacts. The Maillard symposium was held to draw together disparate themes from the food literature (chemistry, physiology, food technology), until then spread across various different meetings focused on aspects of food, and bridge the gaps between different categories of scientist by focusing on the reaction itself and catalyzing interaction between researchers who would not hitherto have exchanged ideas. Much was already known about the chemistry of the low molecular weight components and the impact of the reaction on the nutritional quality of food. Methods to reduce browning and nutritional impairment by either programmed processes or use of inhibitory substances such as sulfite were established. There was also interest in the anti-oxidant properties of MRPs. However, research on the absorption and metabolism of MRPs was in its infancy.

The second symposium had similar themes to the first, but the emphasis included an analysis of polysaccharides and proteins as well as small molecule chemistry (Waller & Feather, 1982). The focus was very much still on food chemistry—both beneficial and negative impacts. The Maillard symposium was held to draw together disparate themes from the food literature (chemistry, physiology, food technology), until then spread across various different meetings focused on aspects of food, and bridge the gaps between different categories of scientist by focusing on the reaction itself and catalyzing interaction between researchers who would not hitherto have exchanged ideas. Much was already known about the chemistry of the low molecular weight components and the impact of the reaction on the nutritional quality of food. Methods to reduce browning and nutritional impairment by either programmed processes or use of inhibitory substances such as sulfite were established. There was also interest in the anti-oxidant properties of MRPs. However, research on the absorption and metabolism of MRPs was in its infancy.

The third symposium (Fujimaki, Namiki, & Kato, 1986) was similar. The fourth symposium (Finot, Aeschbach, Hurrell, & Liardon, 1990) was held at the Nestle Research Centre at Lausanne and included a large number of industrial food scientists. However, a new focus on the reaction in vivo and its role in ageing was beginning to develop, and there was a clear synergy in place between the science of the reaction in vivo and in vitro. By the fifth...
symposium (Labuza, Reineccius, Monnier, O’Brien, & Baynes, 1994) there were two clear themes of Maillard research—medicine and food, a trend that has continued through to the current symposium (Baynes et al., 2005; Horiuchi, Taniguchi, Hayase, Kurata, & Osawa, 2002; O’Brien, 1998). However, in the Eighth Symposium there was an increasing flux of delegates between the medical and food sessions, reflecting the common themes that have emerged in health and nutrition.

Maillard chemistry is still a growing field

The Maillard reaction in food has a long history and has made a substantial impact on food science, especially in recent years. After Maillard’s initial observations in 1912 (Maillard, 1912), the reaction was all but ignored until the 1940s, when research began in earnest. The classic 1953 Hodge paper proposing a set of pathways for the Maillard reaction (Hodge, 1953) was the most cited ever in the Journal of Agricultural and Food Chemistry (Labuza et al., 1994). Since that seminal contribution, the importance of Maillard chemistry in food science, nutrition and medicine remains undisputed, and the field continues to grow (Fig. 1).

The Maillard reaction in food

Nearly 100 years since L.-C. Maillard first reported his observations on colour formation in an aqueous solution of sugar and amino acid (Maillard, 1912), important work that food scientists have played in unraveling the details of the Maillard reaction can be categorized as follows (Finot, 2005):

1. elucidating the chemistry of the reaction, to identify the various pathways,
2. evaluating the impact of different reaction parameters (pH, temperature, time, sugar reactivity, reagent concentration, water activity and glass transition temperature) on the reaction during food processing,
3. quantifying nutritional damage in terms of loss of availability of essential amino acids, particularly lysine,
4. pharmacokinetics,
5. toxicological impact of Maillard reaction products and their role in metabolism.

Work continues on elucidation of the reaction pathways, with the bulk of research carried out in laboratories that have access to state-of-the-art equipment for isolation and characterisation of MRPs. With the most common products of Maillard chemistry now identified, the characterisation of MRPs and pathways is increasingly limited by technology. Huge advances have been made, especially in German laboratories where new methodologies continue to be developed that rely on innovative use of new advances in NMR and MS–MS technology. These are discussed later in this review (see Methodological advances).

Far less research is being carried out on the evaluation of processing parameters on the Maillard reaction, the nutritional damage to proteins due to the Maillard reaction and pharmacokinetics. The emphasis in 2004, when consumers are increasingly aware of the potential of food processing to lower the nutritional quality of food, has shifted far more towards the potential toxicological consequences of this chemistry in consumed products.

Food processing and food technology

Researchers such as Hofmann continue to carry out comprehensive studies of the identification and characterisation of flavour and odour compounds in food chemistry (Hofmann, 2005). Such state-of-the-art analysis includes the use of novel screening techniques that combine instrumental analysis with human psychophysics, LC–MS, 1D and 2D NMR experiments, as well as $^{13}$C labelling techniques. These advanced methodologies have enabled new fields of research such as comparative taste dilution analysis, in

![Fig. 1](http://example.com/figure1.png)

Fig. 1. The number of papers published that include the word ‘Maillard’ (light columns) or glycation (dark columns) in the title, keywords, or abstract 1994–2004. Source, web of science.
which compounds that modify flavour, whilst having no actual taste in isolation, can be detected. This research builds on well established methods to evaluate the taste activity value and odour activity value of individual Maillard reaction products (Hofmann, Ottinger, & Frank, 2004).

**A shift in emphasis towards nutrition: AGEs—risk or benefit?**

An increasing amount of research involves an analysis of whether MRPs, particularly advanced glycation end-products (AGEs), represent a risk or a benefit when consumed in the diet. Research has focused for many years on the potential of certain heterocyclic products of the Maillard reaction, for example meIQ and PhIP, as potential mutagenic compounds if consumed in the diet (Bordas, Moyano, Puigou, & Galceran, 2004; Faist & Erbersdobler, 2002; Felton & Knize, 1998; Murkovic, 2004; Shin, 2003; Shin, Park, & Park, 2003; Taylor et al., 2004). Similarly, the potential of other MRPs to act as anti-oxidants, or provide other beneficial effects, has been noted (Dittrich et al., 2003; Faist & Erbersdobler, 2002; Lee & Shibamoto, 2002; Manzocco, Calligaris, Mastrocola, Nicoli, & Lerici, 2000; Morales & Babbel, 2002; Morales & Jimenez-Perez, 2004), with only a few groups explicitly considering both positive and negative impacts (Faist & Erbersdobler, 2002; Somaza, 2005).

Contemporary research in this field takes one of two approaches. In the first approach, the balance of risk and benefit of AGE consumption is assessed, typically in feeding trials involving consumption of a high dose of a heterogeneous mixture of AGEs, and the physiological effects monitored. In the second approach, new AGEs are identified and/or the specific impact of a specific AGE is monitored. One Maillard reaction product that has attracted effects monitored. In the second approach, new AGEs are identified and/or the specific impact of a specific AGE is monitored. One Maillard reaction product that has attracted attention due to impaired proteolysis. Differences between the Amadori products were not recovered, for example, perhaps 100% recovered in the urine. Protein bound pentosidine and continuous excretion occurs. Not all of the MRPs were MRPs observed in urine are derived from the diet, and that were introduced into the diet. This suggests that most of the MRPs is also surprisingly incomplete (Goldberg et al., 2004). We know that levels of protein-bound MRPs are high in milk products, and are also found in bakery goods, roasted meat (to an extent) and coffee, but the data are by no means comprehensive. Thus, a study of healthy volunteers was undertaken. The volunteers were placed on an MRP-free diet of uncooked food for several days, before being placed on a diet high in MRPs for several days (pretzels or milk products or coffee of defined fructose–lysine, pyralline and pentosidine content, measured as both free and protein bound). The urine of the volunteers was monitored and a significant drop in MRPs was observed during the MRP-free diet phase of the trial, which increased again once MRPs were introduced into the diet. This suggests that most of the MRPs observed in urine are derived from the diet, and that continuous excretion occurs. Not all of the MRPs were 100% recovered in the urine. Protein bound pentosidine and Amadori products were not recovered, for example, perhaps due to impaired proteolysis. Differences between the excretion rate of individual compounds points to individual resorption and metabolic pathways for each specific MRP. A huge amount of work remains to be done to identify the metabolic fate of each compound, and estimate the risk or
benefit, if any, associated with ingestion of each one. Thus, we are starting to see a physiological impact of MRPs, but we do not yet have sufficient data to ascribe specific physiological consequences to the presence of particular MRPs in the diet.

**Fear of frying?**

The recent flurry of publicity regarding the presence of acrylamide in foods, which some argue is a consequence of the Maillard reaction, provides an excellent example of the need to assess the toxicological consequences of the Maillard reaction during food processing. This area has been usefully reviewed recently (Blank, 2005; Taeymans et al., 2004) and is summarised here, in brief.

Acrylamide is soluble in water and reacts with acids, bases and oxidising agents, making it a highly reactive molecule in biological systems, including foods. It is susceptible to epoxidation and Michael addition and can form covalent adducts with DNA and proteins, which suggests that biomarkers such as reacted haemoglobin may prove useful in identifying cases of exposure. However, only DNA adducts have thus far been found and characterised *in vivo*.

There is no doubt that acrylamide is a toxic moiety, but whether it is generated in processed food in sufficient quantities to cause concern remains uncertain. The molecule is a well known neurotoxin following occupational exposure, being mutagenic and carcinogenic following long-term exposure. Acrylamide is classed as a group 2A carcinogen (‘probably carcinogenic’). It is not teratogenic. Exposure can be high in certain occupational environments, but is low for most members of the public, the main exposure coming from packaging materials. It is estimated that the average consumer might consume 35 μg/day from the diet, with this figure rising to thrice this amount for young adults who consume a high proportion of fried food in their diet. However, there is, to date, no direct evidence that any harmful effects have been caused by the presence of this molecule in food (Blank, 2005).

Recent work of several researchers in this area (Mucci, Dickman, Steineck, & Adami, 2003; Mucci, Dickman, Steineck, Adami, & Augustsson, 2003; Mucci, Lindblad, Steineck, & Adami, 2004; Pelucchi et al., 2003; Pelucchi, La Vecchia, Fransechi, & Levi, 2004) has highlighted the urgent need for a validated reference method for the detection of acrylamide in foodstuffs. Current methods have been reviewed by Wenzl, de la Calle, and Anklam (2003), and rely on analysis via GC–MS isotope dilution assay against internal standards, or LC–MS technology. Using these methods, acrylamide has been detected in chips, biscuits, etc., but traces have yet to be reported from boiled food, even if the precursors are present, because the temperature of processing is not sufficiently high. Delatour, Perisset, Goldmann, Riediker, and Stadler (2004), have reported a new analytical method, with a detection limit of 5 μg/kg. This is currently the most sensitive detection method.

There are various hypotheses put forward to explain the presence of acrylamide in foods and studies underway to distinguish between them. Stadler et al., (2002), Stadler et al. (2004), Gertz and Klostermann (2002) and Yasuhara, Tanaka, Hengel, and Shibamoto (2003), have proposed lipid oxidation to play a key role, whereas others have cited the importance of asparagines and Maillard type chemistry (Granvogl, Jezussek, Koehler, & Schieberle, 2004; Mottram, Wedzicha, & Dodson, 2002; Yaylayan, Wnorowski, & Locas, 2003; Zyzak et al., 2003). Papers in this field are appearing at a very rapid rate, as more mechanistic theories are proposed and tested (Rydberg et al., 2003; Taubert, Harlfinger, Henkes, Berkels, & Schomig, 2004) but no definitive picture has yet emerged. It seems likely that there is more than one potential mechanism via which acrylamide can be formed during food processing, and that the precise mechanism of formation will depend on the particular processing regime that a foodstuff undergoes.

**The Atkins’ diet and Maillard chemistry**

At the Eighth Symposium, Beisswenger and co-workers presented some fascinating work on the impact of the Atkins’ diet, from the perspective of Maillard chemistry (Beisswenger, Delucia, Lapoint, Sanford, & Beisswenger, 2005). There is a paucity of clinical data available to assess the safety of this diet, in general terms (Astrup, Larsen, & Harper, 2004). The Atkins’ diet prescribes that less than 20 g fat be consumed per day, forcing the body to burn fat and enter a metabolic state known as ketosis. Ketosis leads to an increase in the physiological concentration of methylglyoxal, a known participant in Maillard chemistry *in vivo* and a potent glycolyotoxin (Thornalley, 2003). Thus, one would predict that those who adopt the Atkins’ diet long-term would begin to experience some of the symptoms of accelerated ageing that are commonly seen in diabetics. This prediction was tested in a clinical trial using overweight members of the community that had voluntarily elected to go on the Atkins’ diet. The impact of the diet on the levels of methyl glyoxal and its precursors, acetoacetate and β-hydroxybutyrate (known products of ketosis), were monitored. Methyl glyoxal levels were found to rise significantly, reaching maximal concentrations at 14–20 days. These preliminary data suggest that tissue and vascular damage is a potential risk of adopting the Atkins’ diet.

**Methodological advances**

Increasingly, the characterisation of MRPs depends on new methodologies, which continue to be developed. For example, Schieberle has introduced the CAMOLA technique (carbon modul labeling technique) (Schieberle, Bareth, Fischer, & Hofmann, 2002) as a novel approach to characterizing transient intermediates in the Maillard reaction. The technique employs 13C-labelled carbohydrates
to gain insight into the formation of selected target compounds, by focusing on which pathways may be operating, and which can be ruled out under any particular set of conditions. Davidek has also described the use of radiolabelled substrates to derive mechanistic information, in this case coupled with the use of novel GC–MS methodology in order to explore the role of acetic acid in the Maillard reaction under particular reaction conditions (Davidek, Devaud, Robert, & Blank, 2005).

Ames (2005), Cotham et al. (2003) and Kislinger, Humeny, and Pischetsrieder (2004)) have pioneered the application of proteomics to the Maillard field. As the number of proteomic techniques to analyse post-translational modification of proteins modified in vivo increases, we are increasingly able to apply these techniques to study modifications to proteins that are introduced during food processing. Challenges still remain, particularly in the area of quantification, developing procedures to locate novel modifications, increasing sensitivity, especially for use in proteins extracted from cell lines, and exploring the interplay between structural modification and function. Personalised nutrition is a long-term goal of the application of the proteomics of the Maillard reaction, in both food systems and physiological situations.

Where to now?

Much work remains to be done to complete our picture of the risks and benefits associated with the consumption of MRPs in the diet, and how this relates to their formation and metabolism within the body. Some of this research awaits the advent of more sensitive methodology, to monitor the formation and degradation of trace compounds in food. As a more comprehensive description emerges, it is likely that more traditional research into the impact of different food processing conditions on the course of the Maillard reaction will re-emerge as an important tool for minimizing the production of toxic MRPs and maximizing the yield of beneficial ones. The Maillard reaction in food is thus likely to remain an active area of research for many years to come.

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References


