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Dietary Maillard Reaction Products: Implications for Human Health and Disease

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Abstract: When foods are heat processed, the sugars and lipids react with the proteins they contain via the Maillard and related reactions to form a wide range of products. As a result, the sensory, safety, nutritional and health-promoting attributes of the foods are affected. Reaction products include advanced glycation/lipoxidation endproducts (AGE/ALEs), acrylamide and heterocyclic amines (HAA), all of which may impact on human health and disease. Furthermore, some Maillard reaction products affect the growth of colonic bacteria and thermally-induced modification of dietary protein can affect allergenicity. This paper briefly reviews aspects of the Maillard reaction in food related to human health.

Keywords: Maillard reaction; advanced glycation endproducts (AGEs); advanced lipoxidation endproducts (ALEs); heterocyclic amines; acrylamide; allergenicity; colonic health

Chemistry of the Maillard reaction (MR)

The Maillard reaction (MR) encompasses a complex network of reactions and the chemistry concerned has been reviewed by many authors over the last 60 years (e.g., HODGE 1953; ZHANG *et al.* 2009). In summary, the MR involves the reaction between the carbonyl group of a reducing sugar with a free amino group, typically the ϵ -amino group of lysine residues in protein. The complexity of the reaction network is increased when lipid is present, since lipid peroxidation products with a carbonyl group may take the place of sugar in the reaction. Furthermore, sugars may undergo oxidation to low molecular mass carbonyl compounds, several of which, including methylglyoxal, are highly reactive and may also react directly with sidechains of amino acid residues including arginine and lysine. The complex network of subsequent reactions that include rearrangement, aldol (and retroaldol) condensation, oxidation, hydration (and dehydration), lead to a myriad of Maillard reaction products (MRPs) including components that may impact on human health, such as acrylamide, heterocyclic amines (HAA) and glycation/lipoxidation endproducts

(AGE/ALEs), as well as those that contribute to colour, flavour and texture. In addition, some MRPs promote phase II enzyme activity while others possess antioxidant properties.

Impact of the MR on human health and disease

Up to the 1980's, most research on the MR came from the food science field and concerned flavour, colour and nutritional value of foods. More recently, in response to government agendas, industry drivers, and consumer group interests, the impact of diet on health and disease has received increased research funding and visibility. This changing funding emphasis has impacted on MR research, leading to new knowledge and paving the way to a supply of heat processed food that promotes health while maintaining sensory quality. Nevertheless, it must be recognised that heating food does more than induce the MR. Indigenous heat labile components are lost or undergo reactions. Such components include polyphenols and some vitamins. Bioavailability of nutrients also becomes modified by heat processing and

ARPs (which are pre-AGEs), AGE/ALEs, HAA and acrylamide have all been investigated for their absorption, metabolism and bioactivity.

AGE/ALEs

Endogenously formed AGE/ALEs are pro-oxidative and pro-inflammatory. Therefore, the impact of dietary AGE/ALEs on health and disease has attracted attention. The metabolic transit of dietary ARPs and AGEs has been reviewed (AMES 2007). The human body handles various AGE/ALEs differently, no doubt due to the diversity of chemical structures involved. Some AGE/ALEs are absorbed into the bloodstream while others remain in the GI tract. There is a lack of well-designed studies concerning the bioactivity of dietary AGEs. Some papers attribute postprandial rises in insulin resistance, plasma isoprostanes and markers of inflammation to increases in serum AGE levels following consumption of thermally processed diets. However, the minor dietary components profile and antioxidant capacity of the high and low AGE diets are frequently not reported but may be expected to differ and could be responsible for the observed effects. In contrast, a dietary intervention randomised crossover study involving feeding male adolescents either a low MRPs or a high MRPs diet for two weeks, SEIQUER *et al.* (2008) demonstrated that there was no effect on various plasma markers of oxidative damage or antioxidant defence. In fact, the high MRP diets possessed higher *in vitro* antioxidant activity and post-intervention erythrocyte samples subjected to oxidation revealed higher antioxidant capacity following the high MRP diet.

HAA

The relationship between heterocyclic aromatic amines (HAA) and human health has been reviewed (e.g., CHENG *et al.* 2006; ALAEJOS *et al.* 2008). HAA are formed at ppb levels in heated muscle tissue, e.g. roasted meat, grilled fish as a result of interactions between amino acids, sugars and creatinine and contribute to the genotoxic or carcinogenic load within the colon. The most common HAA in cooked meats are 2-amino-1-methyl-6-phenylimidazo [4,5-*b*]pyridine (PhIP) and 2-amino-3,8-dimethylimidazo [4,5-*f*]quinoxaline (MeIQx) and it is estimated that between 43 and

110 ng PhIP and 14–47 ng MeIQx are ingested per day for those on a typical Western style diet. Intake of HAA is associated with frequency of consumption of red meat and very well cooked meat, but consumer genotype related to HAA metabolism may also be a factor in cancer risk (ALAEJOS *et al.* 2008).

Acrylamide

The Maillard reaction can lead to acrylamide formation in food, and this has received much attention in the last six years (ZHANG & ZHANG 2007). Acrylamide is carcinogenic in experimental rats and mice and is classed as 'probably carcinogenic' in humans. There are various mechanisms of formation of acrylamide, several involving the Maillard reaction (STADLER & SCHOLZ 2004; ZHANG & ZHANG 2007). Asparagine is key to its formation. Highest levels (several hundred µg/kg) of acrylamide have been reported in foods including potato crisps, coffee and crispbread (STADLER & SCHOLZ 2004). Various steps may be taken to minimise levels of acrylamide in food (e.g., ZHANG & ZHANG 2007; SEAL *et al.* 2008). The real risk to human health of diet-derived acrylamide remains unclear; but a framework for assessing the risk has been published (DYBING *et al.* 2005). Important considerations are its fate in the intestine and any interactions with food matrices that might affect its bioavailability. The metabolite of acrylamide, glycidamide, can form adducts with haemoglobin and DNA. Several large scale epidemiological studies have reported no link between dietary acrylamide and cancer, but one prospective study has reported a link between dietary acrylamide intake and endometrial and ovarian cancer (but not breast cancer) in postmenopausal women (HOGERVORST *et al.* 2007).

Allergen formation and suppression

Recent years having seen growing interest in the role of the MR in dietary protein allergenicity. Roasting peanuts leads to increased allergenic potential due to AGE formation on the allergens, possibly leading to new IgE binding sites (MALEKI *et al.* 2000). In contrast, glycation of proteins of soybeans (VAN DE LAGEMAAT *et al.* 2007) and buckwheat (NAKAMURA *et al.* 2008) leads to re-

duced allergenic potential, assessed by *in vitro* methods. In these examples, the allergen is presumably masked by MR-induced modifications. Since the allergenic response to food allergens can be severe, simple and inexpensive means of reducing the problem, such as common food processing operations are attractive but require more work to engineer desirable outcomes.

Effects on colon health

A 47% increase in faecal nitrogen in adolescent males followed consumption of a heavily heated diet compared to a mildly heated diet, the difference being attributed to heat-induced protein-sugar reactions (SEIQUER *et al.* 2006). AGE/ALE-modified protein is less readily digested, leading to an elevated level of protein residues in the colon and a modified colonic microflora. For example, we have used validated colonic models to demonstrate that, compared to untreated protein, glycated protein modulated the gut microbiota of ulcerative colitis (UC) patients towards a more detrimental community structure, with significant increases in putatively harmful bacteria (clostridia, bacteroides and sulfate reducing bacteria) and decreases in dominant and putatively beneficial bacteria (eubacteria and bifidobacteria) (MILLS *et al.* 2008). AGEs may also ligate the receptor for AGEs (RAGE), initiating a cascade of pro-inflammatory pathways, providing another possible mechanism for the inflammatory response in UC patients.

Conclusion and requirements for future work

Although the MR generates several dietary components that may be detrimental to health, it is also a source of compounds with beneficial health attributes. Furthermore, it is a key source of flavour and colour compounds that are responsible for the enjoyment of most heat processed foods and beverages. A holistic research approach is needed so that as more knowledge is generated concerning the health impact of MRPs, work on the sensory attributes of the foods that contain them is not forgotten.

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