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Review

Food-derived 1,2-dicarbonyl compounds and their role in diseases

Michael Hellwig[a,*], Sabrina Gensberger-Reigl[b], Thomas Henle[a], Monika Pischetsrieder[b]

[a] Chair of Food Chemistry, Technische Universität Dresden, D-01062 Dresden, Germany
[b] Food Chemistry Unit, Department of Chemistry and Pharmacy, Emil Fischer Center, Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU), Nikolaus-Fiebiger-Straße 10, D-91058 Erlangen, Germany

ABSTRACT

Reactive 1,2-dicarbonyl compounds (DCs) are generated from carbohydrates during food processing and storage and under physiological conditions. In the recent decades, much knowledge has been gained concerning the chemical formation pathways and the role of DCs in food and physiological systems. DCs are formed mainly by dehydration and redox reactions and have a strong impact on the palatability of food, because they participate in aroma and color formation. However, they are precursors of advanced glycation end products (AGEs), and cytotoxic effects of several DCs have been reported. The most abundant DCs in food are 3-deoxyglucosone, 3-deoxygalactosone, and glucosone, predominating over methylglyoxal, glyoxal, and 3,4-dideoxyglucosone-3-ene. The availability for absorption of individual DCs is influenced by the release from the food matrix during digestion and by their reactivity towards constituents of intestinal fluids. Some recent works suggest formation of DCs from dietary sugars after their absorption, and others indicate that certain food constituents may scavenge endogenously formed DCs. First works on the interplay between dietary DCs and diseases reveal an ambiguous role of the compounds. Cancer-promoting but also anticancer effects were ascribed to methylglyoxal. Further work is still needed to elucidate the reactions of DCs during intestinal digestion and pathophysiological effects of dietary DCs at doses taken up with food and in "real" food matrices in disease states such as diabetes, uremia, and cancer.

1. Introduction

Historically, sugars have been regarded as the "hydrates of carbon" [1] due to their common formula $C_n(H_2O)_n$. Today, the term "carbohydrates" comprises a large group of polyhydroxyaldehydes and −ketones, that can exist from monomeric forms (e.g., glucose) to polymers comprising thousands of monomers (e.g., cellulose). The most abundant sugar monomers in foods are glucose, fructose, and galactose. The reactivity of sugars, mainly of their aldehyde groups, is reduced in aqueous solution due to hydration and (hemi)acetal formation and closely related to the relative amount of their open-chain form [2]. Depending on the reaction conditions, however, sugars can undergo various degradation reactions leading to products that can show high reactivity against biomolecules. The primary targets for enzyme-catalyzed sugar conversion in physiological systems (e.g., for phosphorylation) are the hydroxyl groups. Phosphorylation of hydroxyl groups facilitates C−O bond cleavage and entails many of the chemical degradation reactions of sugar derivatives in physiological media. Further characteristics of carbohydrate degradation *in vivo* are the slightly alkaline, but constant pH of blood and tissues and the relatively low temperature accompanied by potentially very long incubation times (minutes to several decades) [3]. The reaction conditions encountered by carbohydrates during food processing and storage are quite different: In most foods, the pH value is rather acidic and often variable, applied temperatures can be comparatively high (e.g., roasting above 300 °C), but the processing time is short (from seconds up to several hours). Certain processed foods can be stored for several years, allowing specific reactions, because the subcellular compartmentation of reactants in living cells is broken up during processing and thus new reaction partners become of importance during storage. Another particularity of food processing is the application of dry heat, which lowers the water activity in foods or parts of them (bread crust, cookies, grilled meat). In such cases, water cannot longer participate in chemical reactions. Under these extreme conditions, carbohydrates can degrade in the absence of amino compounds in a process called "caramelization" [4], but also in the presence of amino compounds in the Maillard reaction.

* Corresponding author.
E-mail address: Michael.Hellwig@tu-dresden.de (M. Hellwig).

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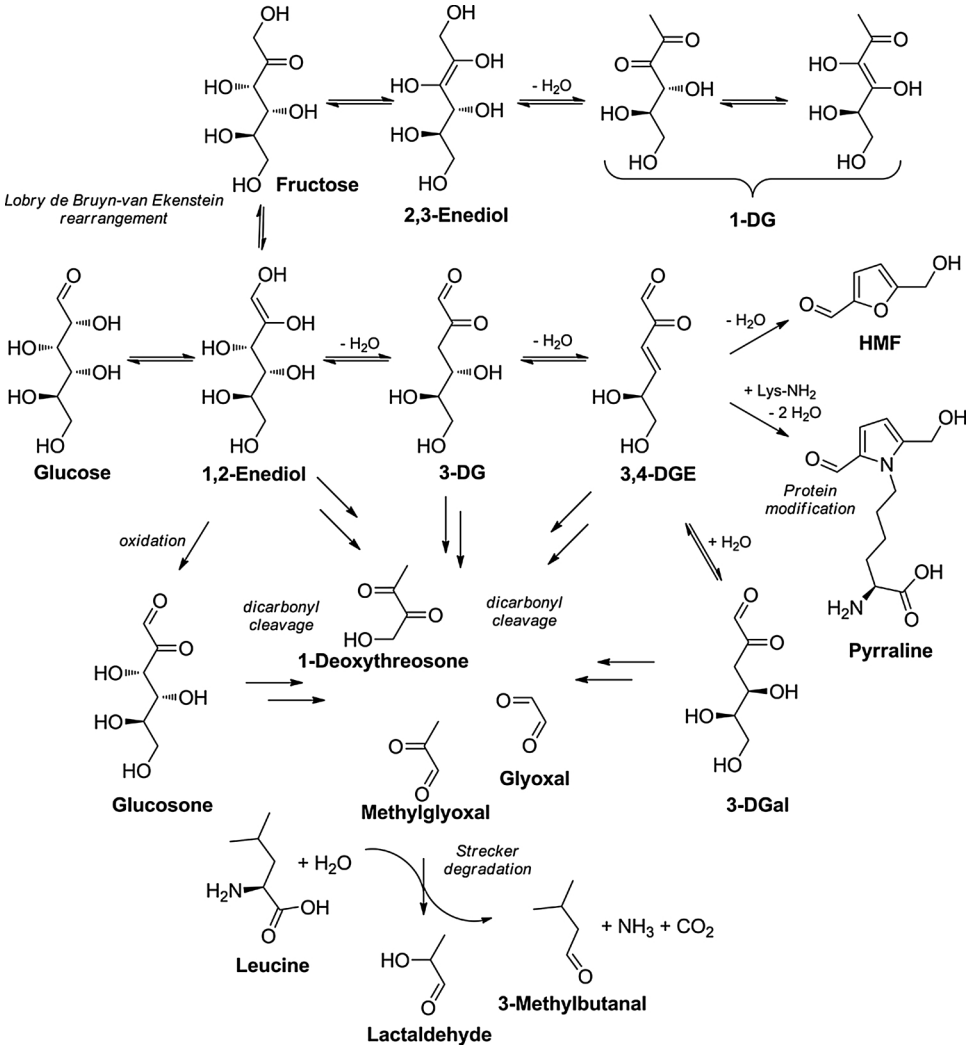

Fig. 1. Proposed degradation reactions of monosaccharides in caramelization and Maillard reactions.

2. Formation and degradation of 1,2-dicarbonyl compounds (DCs) in food

Despite the inapplicable historical designation of saccharides as the hydrates of carbon, the main degradation pathways of carbohydrates are indeed dehydration and redox reactions [4–8]. Tautomerism reactions in the open-chain form of carbohydrates (Fig. 1) can lead to the formation of unsaturated 1,2-diols ("enediols"), that can either react back to the initial sugar, its C2-epimer or the respective ketose, a reaction known as the Lobry de Bruyn–Alberda van Ekenstein rearrangement [9]. By this reaction, glucose is in equilibrium with mannose and fructose. Analogous tautomerism reactions of fructose and other ketoses lead to 2,3-enediols. By successive dehydration steps in the 1,2-enediol, first 3-deoxyglucosone (3-DG) is formed, a ketoaldehyde belonging to the class of 1,2-dicarbonyl compounds (DCs). The following dehydration steps lead to unsaturated osones such as 3,4-dideoxyglucosone-3-ene (3,4-DGE) and further to heterocyclic 5-hydroxymethylfurfural (HMF) [10,11]. In aqueous environments, the dehydration leading to 3,4-DGE is reversible, and 3-DG as well as its C-4 epimer 3-deoxygalactosone (3-DGal) can be formed (3-deoxyhexosone interconversion) [12–14]. Dehydration reactions in 2,3-enediols lead to 1-deoxydiuloses such as 1-deoxyglucodiulose (1-DG) [15]. This substance is termed a "reductone" due to its α-hydroxy diketo structure, which is in tautomeric equilibrium with the respective α-keto enediol structure. A prominent example of a reductone is ascorbic acid. Reductones are also formed through oxidation of 1,2-enediols ("sugar autoxidation") by reactive oxygen species at the double bond—glucosone is directly produced from glucose by this reaction [16,17]. Reductones can easily be oxidized to tricarbonyl compounds and both reductones and their tricarbonyl oxidation products are prone to undergo fragmentation of their carbon skeleton [8,18–20]. Fragmentation reactions of long-chain DCs generate short-chain DCs such as glyoxal (GO) and methylglyoxal (MGO) [21,22]. GO also results from unsaturated fatty acids during lipid peroxidation [23].

Monosaccharides in food are often bound in di-, oligo- and polysaccharides such as maltose, lactose, starch, and inulin. During heating, these saccharides can (i) hydrolyze to the constituting monosaccharides and then undergo degradation reactions as described above, (ii) form degradation products analogous to the monosaccharides, for example 1-deoxymaltosone (Fig. 2) [7], or (iii) participate in particular disaccharide-specific reactions. For example, the pyranone intermediate formed from cyclic 1-deoxymaltosone through dehydration is stabilized by the glucose substituent thereby allowing the formation of significant amounts of the aroma compound maltol (Fig. 2), which is not formed from glucose [24]. Other examples for oligosaccharide-specific reactions are the successive detachment of 1,4-dideoxyglucosone or 4-deoxyglucosone units from the reducing end ("peeling-off" mechanisms) [25,26]. Saccharose as a non-reducing disaccharide cannot form enediols, and the formation of DCs from this sugar is strongly limited. Therefore, saccharose is a suitable ingredient to suppress Maillard and caramelization reactions in food.