ACS FOOD SCIENCE & TECHNOLOGY

pubs.acs.org/acsfoodscitech

Article

Occurrence of Genotoxic Furan-2(5*H*)-one in Heated Milk and Pancakes: Key Role of Lactose and Free Radicals during Cooking

Alexandre Dusart, Constance Hermans, and Sonia Collin*

Cite This: https://doi.org/10.1021/acsfoodscitech.6c00226

Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: Furan-2(5*H*)-one is a genotoxic α,β-unsaturated lactone occurring naturally in heat-processed foods. Its formation pathways in food systems remain poorly understood. This study combines analyses of commercial milks and model systems to evidence which factors influence their synthesis, with a special focus on furfuryl alcohol as the key intermediate. Although the threshold of toxicological concern for furan-2(5*H*)-one is 0.15 μg person^{-1}·day^{-1}, growing-up cow milks and chocolate drinks were found to contain up to 383 and 521 μg·kg^{-1}, respectively, versus <50 μg·kg^{-1} in soy-based alternatives. Under severe heating conditions (133 °C, 20 min), furan-2(5*H*)-one levels reached 5741 μg·kg^{-1} in cow milk, significantly exceeding the levels measured in lactose-free milk (266 μg·kg^{-1}). Pancakes prepared with lactose-containing milk similarly exhibited substantially higher concentrations (650 μg·kg^{-1}) than their lactose-free counterparts (26 μg·kg^{-1}). Results obtained with aqueous model systems demonstrated the pivotal role of disaccharides and Fenton reagents in furan-2(5*H*)-one formation. Our data raise concerns regarding the occurrence of this compound in other thermally processed foods.

KEYWORDS: *furan-2(5H)-one, genotoxicity, dairy products, 1,4-linked disaccharide, Fenton reaction*

1. INTRODUCTION

Furan-2(5*H*)-one (hereafter abbreviated as F2(5*H*)one) is an α,β-unsaturated lactone with a characteristic buttery odor. In 2019, the European Food Safety Authority (EFSA) evaluated it and identified it as genotoxic *in vivo*.[1] It was subsequently removed from the list of authorized flavoring substances.[2] However, F2(5*H*)one remains present in food, not as a flavoring substance but as a compound most presumably formed during thermal processing. Recent monitoring studies have revealed this compound in a variety of heat-treated commercial sweet snacks, at concentrations exceeding the mg·kg^{-1} level in certain cakes.[3] Considering the very low threshold of toxicological concern (TTC) for genotoxic substances (*i.e.*, 0.15 μg·person^{-1}·day^{-1}), these levels mean that to avoid F2(5*H*)one genotoxic effects, the maximum daily consumption should not exceed 150 mg of pancake.

A few synthesis pathways starting from maltose- and glucose-derived intermediates have been proposed.[4−7] More recently, a correlation was observed between furfuryl alcohol (FOL) levels and F2(5*H*)one in commercial sweet snacks, suggesting that F2(5*H*)one may be formed through oxidation of FOL to furfural (FAL), followed by decarboxylation of furoic acid (part C of Figure 1).[3,8,9]

FOL and FAL are produced in significant amounts from sugars, particularly 1,4-linked disaccharides rather than monosaccharides.[10] Following condensation between the disaccharide and a primary amine (part A of Figure 1), enolization of the resulting Amadori compound yields the 2,3-enediol intermediate. Subsequent β-elimination of the sugar moiety, facilitated by coplanar alignment of the C1−C4 glycosidic bond, generates the 1-imino-3-keto structure.[11,12] Retro-Claisen condensation at position C1 yields 1,4,5-trihydroxypent-1-en-2-olate, also known as 3-deoxypentose (3-DP) under mildly acidic conditions.[12−17] This compound can further cyclize and dehydrate to FOL (part B of Figure 1).[13] Under oxidative conditions, 1,4,5-trihydroxypent-1-en-2-olate instead forms 3-deoxypentosulose (3-DPS), which can undergo cyclization and dehydration to form FAL.[13] The reported 3-DPS formation from 1,4-linked disaccharides, rather than from monosaccharides, suggests that this pentose-derived intermediate constitutes a key branching point in FOL and FAL formation.[12,13,18,19]

In addition to their formation from disaccharides, FOL and FAL can also be generated, to a lesser extent, from monosaccharides (part D of Figure 1). This occurs through cyclization and dehydration of key intermediates 2-deoxypentose (2-DP) and 3-deoxyglucosone (3-DG), respectively.[18,20−23] However, these pathways are minor, 3-DG leading more easily to 5-hydroxymethylfurfural (5-HMF).[11,20]

Food matrices subjected to heat treatment (*e.g.*, pasteurization, sterilization) and containing 1,4−linked disaccharides are particularly prone to forming FOL.[10] Schöpf *et al.* showed, for example, FOL levels were 3 times as high in porridge made with lactose-free cow milk spiked with lactose (galactose (β1 → 4) glucose) than in porridge made with lactose-free milk.[24] In roasted coffee, rich in β1 → 4 polysaccharides such as cellulose, FOL levels can reach up to 800 mg·kg^{-1}.[25]

Received: February 25, 2026
Revised: July 15, 2026
Accepted: July 27, 2026

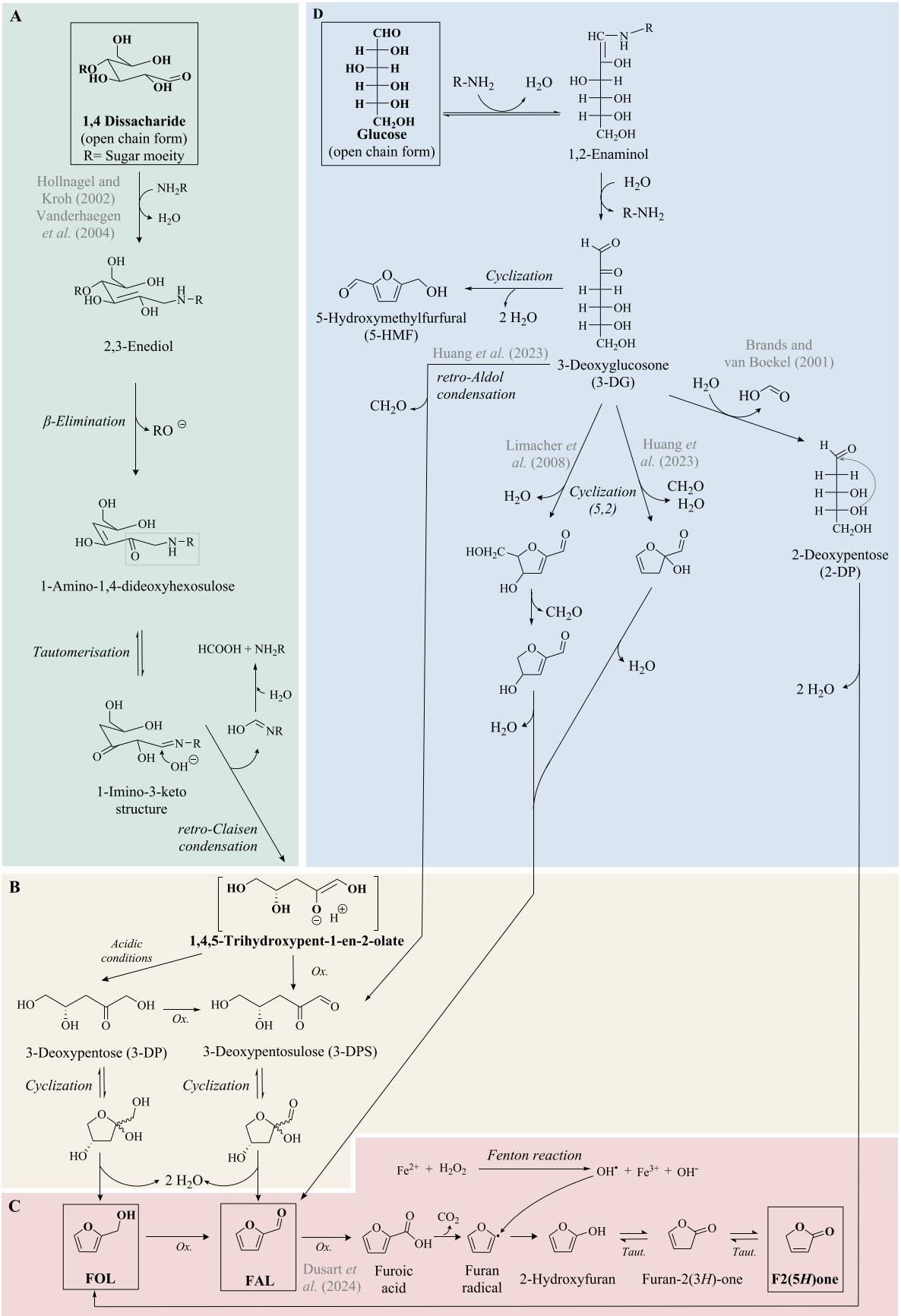

Figure 1. Proposed formation pathways of furfuryl alcohol (FOL) and furfural (FAL) from 1,4-linked disaccharides (part A and B) and monosaccharides (part D and B), and their subsequent conversion to furan-2(5H)-one (F2(5H)one, part C). Ox., oxidation; Taut., tautomerization.

https://doi.org/10.1021/acsfoodscitech.6c00226
ACS Food Sci. Technol. XXXX, XXX, XXX−XXX

Although the formation of furfural and furfuryl alcohol from sugars—particularly 1,4-linked disaccharides—has been extensively documented, the formation of genotoxic F2(5*H*)one from these potential precursors has not been explored to date. The present study addresses this gap by examining F2(5*H*)one formation from sugars during thermal processing, through the combined use of dairy matrices and complementary model systems.

2. MATERIAL AND METHODS

2.1. Chemicals

The following chemicals were used: 2-acetylthiophene (99%, Merck), D-(+)-galactose (99%, Janssen Chemical), D-(+)-glucose (>99%, Fluka), dichloromethane (>99.8%), furan-2(5*H*)-one (96%, α Aesar), furfural (≥98%, Sigma-Aldrich), furfuryl alcohol (99%, Sigma-Aldrich), hydrogen peroxide (35%, Merck), iron(II) sulfate heptahydrate (99,7%, VWR chemicals), lactose (LactoFerm, 96%), maltose (99%, DIFCO), and *n*-decane (99%, Merck).

2.2. Samples

2.2.1. Commercial Dairy Products. Twenty-two commercial dairy products, including national and distributor brands, were purchased from Belgian supermarkets between January 2020 and April 2025.

2.2.2. Milk Heating Procedures. Milks were subjected to four thermal conditions: (1) No heating (room temperature); (2) heating to 60 °C for 20 min (t_0 = start of heating); (3) boiling in an open saucepan for 20 min (t_0 = start of heating); (4) autoclaving (ramp to 133 °C, 20 min plateau, followed by cooling). The autoclaving was used to maximize the reactivity of potential furan-2(5*H*)-one precursors under controlled and highly reproducible conditions.

After cooling, the autoclaved milks exhibited a flan-like texture and were therefore homogenized with an Ultra-Turrax. The device was then rinsed with 20 mL demineralized water to recover any remaining residues.

2.2.3. Laboratory-Made Pancakes. Two batches of pancakes were prepared: one with usual lactose-containing (L) cow milk, and the other with lactose-free (LF) cow milk, both semiskimmed and UHT. The batter was composed of 300 g wheat flour, 520 g milk, and 3 eggs. After homogenization of the batter, portions of approximately 70 g were taken and cooked in a nonstick pan, for about 1 min and 30 s on the first side and 45 s on the second. The first two pancakes of each production batch were discarded.

2.2.4. Aqueous and Thermal Models. Aqueous model systems (50 g) were prepared with demineralized water containing either lactose (50 g·L^{-1}), maltose (50 g·L^{-1}) or a mix of galactose and glucose (both at 25 g·L^{-1}). In Fenton models, 1 g·L^{-1} H_2O_2 and 3 mg·L^{-1} Fe^{2+} were added to the previously described models. Models were all prepared in 250 mL Schott glass bottles with loosely closed caps to prevent overpressure during heating. Heating was done in an autoclave (Raypa steam sterilizer) with a ramp to 133 °C, a 20 min thermal plateau, and subsequent cooling. Samples were then rapidly cooled in a running water bath.

2.3. Isolation of Flavoring Substances

For pancakes, approximately 100 g of the sample was frozen in liquid nitrogen, crushed in a mortar, then ground with a grinder (Bosch KM13). A 30 g portion of the resulting powder was weighed and spiked with 150 μL of internal standard (IST, 2-acetylthiophene 8 mg·L^{-1}, concentration in sample after spike 40 μg·kg^{-1}). Solid−liquid extraction was performed using bidistilled dichloromethane (2 × 50 mL, 20 min mixing), followed by filtration through a Büchner equipped with glass fiber filters. The combined organic extracts were dried over Na_2SO_4 before being transferred to the Solvent-Assisted Flavor Evaporation (SAFE) dropping funnel.

Model systems samples (50g) were spiked with 150 μL of IST (2-acetylthiophene 8 mg·L^{-1}, concentration in sample after spike 24 μg·kg^{-1}) and extracted with bidistilled dichloromethane (2 × 50 mL, 1 min stirring), before being dried over Na_2SO_4. The combined organic extracts were dried over Na_2SO_4 and subjected to SAFE distillation as follows: water bath temperature: 40 °C; pressure below 10^{-3} Pa; apparatus body at 30 °C, distillate recovered in the liquid nitrogen-cooled flask for 25 min. The distillate was finally dried with anhydrous Na_2SO_4.

Liquid dairy products samples (50g) were spiked with 150 μL of IST (8 mg·L^{-1}, concentration in sample after spike 24 μg·kg^{-1}) and were first SAFE distilled before extraction with bidistilled dichloromethane (3 × 25 mL, 1 min stirring), and dried over Na_2SO_4.

All final organic extracts were spiked with 25 μL of *n*-decane (50 mg·L^{-1}) as external standard (EST), before concentration to 500 μL using a Kuderna-Danish concentrator at 45 °C and stored at − 80 °C prior to GC-MS analysis. The IST/EST peak area ratio was checked as a quality control measure.

2.4. Gas Chromatography/Mass Spectrometry

Gas chromatographic analyses of the SAFE extracts were carried out using an Agilent 7890B gas chromatograph (Agilent, Belgium) coupled to a single quadrupole mass spectrometer (Agilent 5977B). Extracts (1 μL) were injected in splitless mode (front inlet: 250 °C; splitless hold time: 0.8 min). Compound separation was achieved on a nonpolar CP-Sil 5 CB capillary column (50 m × 0.32 mm i.d., 1.2 μm film thickness; Agilent, Belgium). Helium (99.999% purity) connected to a carrier gas filter (Agilent CP17973) was used as the carrier gas at a constant pressure of 100 kPa. The oven temperature was initially held at 36 °C for 2 min, then increased to 95 °C at 23.6 °C·min^{-1} (2 min hold), followed by a ramp to 130 °C at 17.5 °C·min^{-1} (15 min hold), and finally raised to 250 °C at 20 °C·min^{-1}, with a final hold of 28 min. The GC was connected to the mass spectrometer via a transfer line maintained at 250 °C. Electron impact ionization (70 eV) was applied, and data were acquired in selected-ion monitoring (SIM) mode. Supporting Information includes mass spectral data and retention indices (Table S1).

2.5. Identification and Quantification

After an external calibration relative to the IST with FOL, FAL, and F2(5*H*)one analytical standards (at the expected concentration ranges in the extracts), the following equation was used for quantification in the samples of the media models: [analyte X, in μg·kg^{-1}] = [IST, in μg·kg^{-1}] × (IST response coefficient/X response coefficient) × (X area/IST area). For each compound, the linearity of the relative response was verified with Mandel's fitting test (R^2 > 0.99). For commercial dairy products, F2(5*H*)one was instead quantified by standard addition, with fortification levels adapted to the expected concentrations in the samples. The concentration of F2(5*H*)one was thus determined as follows in the samples: [F2(5*H*)one, in μg·kg^{-1}] = [IST, in μg·kg^{-1}] × (1/slope of standard addition curve relative to IST) × (F2(5*H*)one area/IST area). Calibration and standard addition curves are presented in the Supporting Information (Figure S1).

The method was validated in terms of linearity, matrix effect, repeatability (CVr) and within-lab reproducibility (CV_{RW}). Limits of detection (LOD) and quantification (LOQ) of the method were estimated using a signal-to-noise (S/N) approach, in food samples with low amount of the analytes to account for matrix effects and extraction losses. The LOD and LOQ were defined as the concentration in the sample giving a S/N ratio of 3 and 10 respectively. Validation results are provided in Supporting Information 2 (Table S2).

2.6. Statistical Analysis

Boxplots were used to display the distribution of FOL, FAL, and F2(5*H*)one concentrations across different categories of dairy and plant-based beverages (*e.g.*, chocolate milk, soy-based drinks). For groups with at least two samples, boxplots show the median (center line), first and third quartiles (box edges), and whiskers extending to 1.5 times the interquartile range. For categories represented by a single sample (n = 1), the measured value was shown as a diamond marker.

https://doi.org/10.1021/acsfoodscitech.6c00226
ACS Food Sci. Technol. XXXX, XXX, XXX−XXX

Table 1. Concentrations of Furfuryl Alcohol (FOL), Furfural (FAL), and Furan-2(5*H*)-one (F2(5*H*)one) in Commercial Samples[a]

samples	FOL	FAL	F2(5*H*)one
		($\mu g \cdot kg^{-1}$)	
Lactose-containing samples			
Whole cow milk−HTST	<LOD	<LOD	<LOD
Whole cow milk−UHT	12	2	53
Semiskimmed cow milk−UHT	<LOD	<LOD	17
Growing-up milk 1−UHT	4	<LOD	111
Growing-up milk 2−UHT	20	7	132
Growing-up milk 3−UHT	268	22	383
Chocolate cow milk 1−UHT	875	8	325
Chocolate cow milk 2−UHT	1609	13	451
Chocolate cow milk 3−UHT	57	4	52
Chocolate cow milk 4−UHT	25	4	72
Chocolate cow milk 5−UHT	117	5	128
Chocolate cow milk 6−UHT	985	20	383
Chocolate cow milk 7−UHT	1674	31	521
Lactose-free (LF) samples			
LF semiskimmed cow milk−UHT	<LOD	<LOD	14
LF Chocolate cow milk−UHT	101	15	87
Chocolate soy milk 1−UHT	30	<LOD	8
Chocolate soy milk 2−UHT	18	<LOD	9
Chocolate soy milk 3−UHT	28	<LOD	49
Chocolate soy milk 4−UHT	24	<LOD	10
Flavored soy milk (banana) 1−UHT	<LOD	15	13
Flavored soy milk (red fruits) 2−UHT	57	31	6
Flavored soy milk (vanilla) 3−UHT	3	<LOD	5

[a]UHT: Ultrahigh temperature; LOD: Limit of detection.

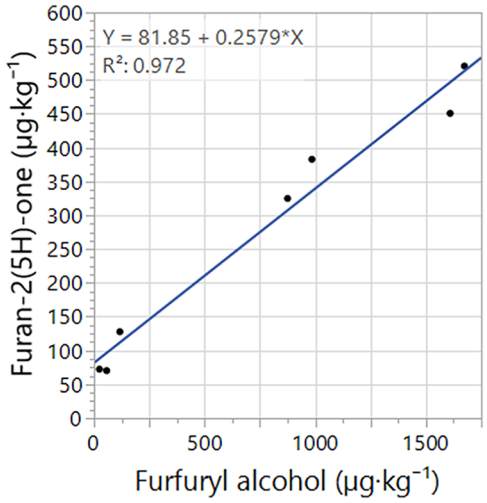

Figure 2. Correlation between furfuryl alcohol and furan-2(5*H*)-one levels ($\mu g \cdot kg^{-1}$) in chocolate cow milks.

3. RESULTS AND DISCUSSION

3.1. FOL, FAL, and F2(5*H*)one in Commercial Milks

FOL, FAL, and F2(5*H*)one levels were first measured in twenty-one commercial milks. As depicted in Table 1, F2(5*H*)one concentrations reached 53 $\mu g \cdot kg^{-1}$ in ultrahigh-temperature-treated (UHT) whole cow milk, while FOL and FAL levels were $12 \cdot kg^{-1}$ and 2 $\mu g \cdot kg^{-1}$, respectively. In contrast, these compounds were undetectable in high-temperature, short-time-treated (HTST) whole cow milk, consistently with previous findings.[26] Intermediate F2(5*H*)one levels were found in both UHT semiskimmed milks (17 and 14 $\mu g \cdot kg^{-1}$ in lactose-containing and lactose-free samples, respectively).

Surprisingly, F2(5*H*)one levels were found to be much higher in the three (semiskimmed) growing-up milks, reaching up to 383 $\mu g \cdot kg^{-1}$. This might be due to their enrichment with metal cations (*e.g.*, iron, magnesium) and vitamins, including ascorbic acid, known to promote hydroxyl radical formation through Fenton reactions.[27,28]

Although chocolate has recently been reported to contain less than 100 $\mu g \cdot kg^{-1}$ F2(5*H*)one, levels up to 521 $\mu g \cdot kg^{-1}$ were found in some chocolate cow milk samples.[3] For these seven commercial products, a strong positive correlation ($R^2 = 0.97$) was observed between FOL and F2(5*H*)one (Figure 2). Given the similar cocoa content (1−5%) across these products, this indicates that cocoa itself is not the key factor explaining the F2(5*H*)one levels, although magnesium could enhance F2-(5*H*)one synthesis.[29] A lactose-free (LF) counterpart of chocolate milk N°7 (same brand, but formulated with lactose-free cow milk) showed markedly lower levels of all three compounds: FOL was more than 16 times lower, FAL was 2 times lower, and F2(5*H*)one nearly 6 times lower.

All the chocolate soy milks also showed much lower levels of F2(5*H*)one (8 to 49 $\mu g \cdot kg^{-1}$). A similar trend was observed for FOL, whereas FAL was not detected in any of these samples. Although the potential impact of other ingredients cannot be entirely excluded and the precise processing conditions remain unknown, compositional differences between traditional milk and soy milk appear to be the key factor explaining the different levels of F2(5*H*)one. Cow milk contains approximately 48 $g \cdot kg^{-1}$ lactose, while soy milk does not contain 1,4-linked disaccharides, but rather raffinose (1.4 $g \cdot kg^{-1}$), sucrose (8.8 $g \cdot kg^{-1}$), glucose (1.3 $g \cdot kg^{-1}$), and fructose (1.3 $g \cdot kg^{-1}$).[27,28]

The three flavored soy milks without chocolate also contained low concentrations of F2(5*H*)one ($\leq$13.0 $\mu g \cdot kg^{-1}$). No substantial differences were noted, except for slightly higher FAL levels in some samples. Figure 3 summarizes all commercial milk samples per milk product category.

3.2. Impact of Heating Lactose-Containing UHT Cow Milks

The commercial semiskimmed milk (UHT) was heated for 20 min at 60 °C, at boiling temperature, or at 133 °C (autoclaved). As depicted in Table 2, autoclaving strongly promoted FOL, FAL, and F2(5*H*)one synthesis (31 478, 454, and 5741 $\mu g \cdot kg^{-1}$, respectively). The autoclaved sample also exhibited noticeable browning. Such high levels were not observed when the same heat treatment was applied to the corresponding semiskimmed LF milk (UHT), commercially produced by enzymatic hydrolysis of lactose to glucose and galactose.

3.3. Impact of the Presence of Lactose in Cow Milk for Pancake Preparation

Pancakes were prepared from eggs, wheat flour, and either lactose-containing (L) or lactose-free (LF) semiskimmed milk (UHT). As depicted in Figure 4, F2(5*H*)one reached 650 $\mu g \cdot kg^{-1}$ in pancakes made with lactose-containing milk, while only 26 $\mu g \cdot kg^{-1}$ was produced with the LF milk counterpart (chromatograms are presented in Figure S2). Similarly, both FOL and FAL showed much lower levels (70 and 8 $\mu g \cdot kg^{-1}$ versus 4588 and 87 $\mu g \cdot kg^{-1}$, respectively). In all samples, FOL was the major compound, followed by F2(5*H*)one and FAL. No detectable level of any of the three target compounds was observed in unheated pancake batter.

https://doi.org/10.1021/acsfoodscitech.6c00226
ACS Food Sci. Technol. XXXX, XXX, XXX−XXX

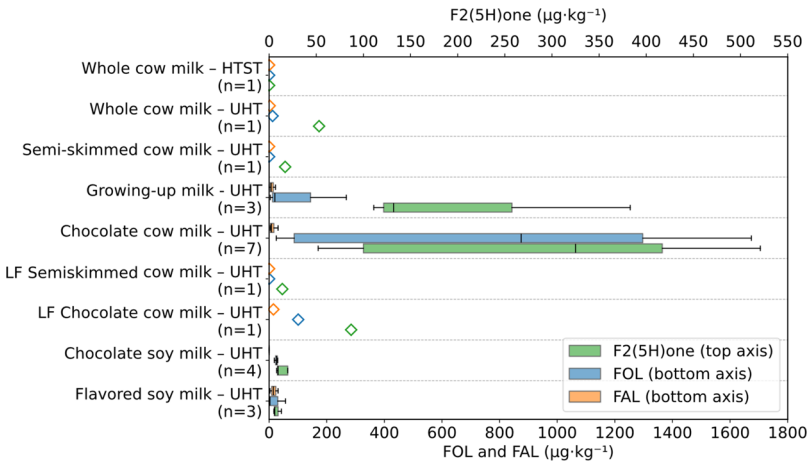

Figure 3. Concentrations of furfuryl alcohol (FOL), furfural (FAL), and furan-2(5*H*)-one (F2(5*H*)one) in various commercial milk samples. For each group ($n \geq 2$), boxplots represent the interquartile range (IQR, 25th−75th percentile), with the horizontal line indicating the median.

Table 2. Concentrations of Furfuryl Alcohol (FOL), Furfural (FAL), and Furan-2(5*H*)-one (F2(5*H*)one) in Heat-Treated UHT Semiskimmed Milks[a]

samples	FOL	FAL	F2(5*H*)one
		($\mu g \cdot kg^{-1}$)	
Semiskimmed milk−UHT			
Room temperature	<LOD[d]	<LOD[b]	17[d]
20 min 60 °C	<LOD[d]	<LOD[b]	11[d]
20 min 100 °C	8[c]	<LOD[b]	43[c]
20 min 133 °C	31 478[a]	454[a]	5741[a]
Semiskimmed lactose-free (LF) milk−UHT			
Room temperature	<LOD[d]	<LOD[b]	14[d]
20 min 133 °C	874[b]	359[a]	266[b]

[a]The relative difference between duplicates was <15%, significantly different results are shown with a distinct letter, the letter "a" being the highest value of the series.

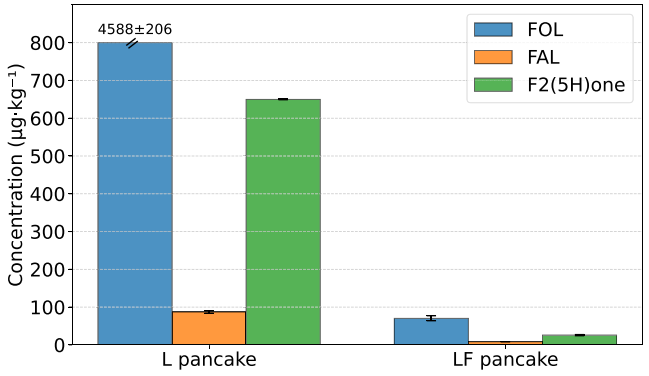

Figure 4. Levels ($\mu g \cdot kg^{-1}$) of furfuryl alcohol (FOL), furfural (FAL), and furan-2(5*H*)-one (F2(5*H*)one) in pancakes prepared with lactose-containing (L) or lactose-free (LF) UHT semiskimmed milk.

3.4. F2(5*H*)one Thermal Synthesis in Aqueous Model Systems Spiked with Different Sugars and Fenton Reagents

Aqueous model systems containing either lactose (concentration: 50 $g \cdot L^{-1}$, close to that of commercial milks), maltose (50 $g \cdot L^{-1}$), or a mixture of glucose and galactose (both at 25 $g \cdot L^{-1}$) were first heated at 133 °C for 20 min. Only trace amounts of F2(5*H*)one were measured, yet with higher levels in disaccharide models (34−46 $\mu g \cdot kg^{-1}$) (Table 3), similar to those measured in commercial UHT milks. Traces of FOL were detected for maltose, while FAL was produced at measurable levels, slightly more from disaccharides (455−508 $\mu g \cdot kg^{-1}$) than from the galactose-glucose mixture (390 $\mu g \cdot kg^{-1}$). These levels are comparable to those found in autoclaved cow milks (Table 2).

Supplementation with Fenton reagents prior to heating strongly increased the formation of all analytes, with up to 876 $\mu g \cdot kg^{-1}$ F2(5*H*)one in lactose model. Yet concentrations remained substantially lower than in heated milks. This difference may be due both to the buffering capacity of milk, previously reported to promote FOL formation, and to the strong oxidative conditions used here, which might enhance F2(5*H*)one degradation.[30] Overall, the Fenton reaction strongly enhanced the formation of all three studied compounds.[31] These results highlight the key role of additional milk components for FOL and F2(5*H*)one synthesis.

In conclusion, thermal processing of lactose-rich foods appears to strongly enhance the synthesis of genotoxic F2(5*H*)one. Incorporating Fenton reagents into model systems confirmed that hydroxyl radicals significantly increase formation not only of F2(5*H*)one but also of its potential precursors FOL and FAL. The F2(5*H*)one level in commercial growing-up cow milks and chocolate dairy drinks warrants concern, whereas soy-based alternatives show moderate levels. Using lactose-free milk for cooking pancakes or other cakes emerges as the easiest way to reduce F2(5*H*)one levels. High temperature treatments, Fenton reagents, and use of the flavoring substances FOL and FAL should also be avoided. Innovative strategies for limiting F2(5*H*)one levels in other heated food ingredients rich in 1,4-disaccharides (*e.g.*, diastatic flours, kilned malts, malt-containing biscuits) should be quickly explored. While the present study identified key 1,4-disaccharide precursors and processing conditions involved in furan-2(5H)-one formation, further mechanistic investigations, including systematic kinetic experiments and isotope-labeled precursor studies, are required to conclusively elucidate the underlying reaction pathway. In parallel, the food matrices identified in this study provide a rational basis for future monitoring efforts, which would generate more comprehensive occurrence data and support dietary exposure assessments.

https://doi.org/10.1021/acsfoodscitech.6c00226
ACS Food Sci. Technol. XXXX, XXX, XXX−XXX

Table 3. Concentrations of Furfuryl Alcohol (FOL), Furfural (FAL), and Furan-2(5*H*)-one (F2(5*H*)one) in Aqueous Model Systems after Heat Treatment (20 min, 133 °C), with (+) or without (−) Fenton Reagents[a]

sample	Fenton	FOL	FAL	F2(5*H*)one
		($\mu g \cdot kg^{-1}$ of aqueous media)		
Lactose (50 $g \cdot L^{-1}$)	−	<LOD[d]	455[c]	34[c]
Maltose (50 $g \cdot L^{-1}$)	−	18[c]	508[c]	46[c]
Galactose (25 $g \cdot L^{-1}$) + Glucose (25 $g \cdot L^{-1}$)	−	<LOD[d]	390[c]	19[d]
Lactose (50 $g \cdot L^{-1}$)	+	1475[a]	18,623[a]	876[a]
Galactose (25 $g \cdot L^{-1}$) + Glucose (25 $g \cdot L^{-1}$)	+	390[b]	11,332[b]	466[b]

[a]Fenton reagents: 3 $mg \cdot L^{-1}$ Fe^{2+} and 1 $g \cdot L^{-1}$ H_2O_2. The relative difference between duplicates was <15%, significantly different results are shown with a distinct letter, the letter "a" being the highest value of the series.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsfoodscitech.6c00226.

Selected ion monitoring (SIM) acquisition windows, mass spectral data, and retention index of monitored volatiles (Table S1); calibration and standard addition curves for furfuryl alcohol, furfural, and furan-2(5*H*)-one (Figure S1); validation parameter results (Table S2); SIM chromatograms of volatile extract from pancakes prepared with lactose-containing milk or lactose-free milk (Figure S2) (PDF)

■ AUTHOR INFORMATION

Corresponding Author

Sonia Collin − *Unité de Brasserie et des Industries Alimentaires, Louvain Institute of Biomolecular Science and Technology (LIBST), Faculté des Bioingénieurs, Université catholique de Louvain, Louvain-la-Neuve 1348, Belgium;* orcid.org/0000-0002-1929-098X; Email: sonia.collin@uclouvain.be

Authors

Alexandre Dusart − *Unité de Brasserie et des Industries Alimentaires, Louvain Institute of Biomolecular Science and Technology (LIBST), Faculté des Bioingénieurs, Université catholique de Louvain, Louvain-la-Neuve 1348, Belgium;* orcid.org/0000-0003-4944-5193

Constance Hermans − *Unité de Brasserie et des Industries Alimentaires, Louvain Institute of Biomolecular Science and Technology (LIBST), Faculté des Bioingénieurs, Université catholique de Louvain, Louvain-la-Neuve 1348, Belgium*

Complete contact information is available at: https://pubs.acs.org/10.1021/acsfoodscitech.6c00226

Funding

This work was supported by the Belgian Federal Public Service of Health, Food Chain Safety and Environment through the contract RT 19/7 FLAVOURAN and RF 25/28 FURANORI.

Notes

The authors declare no competing financial interest.

■ REFERENCES

(1) Younes, M.; Aquilina, G.; Castle, L.; Engel, K.-H.; Fowler, P.; Fernandez, M. J. F.; Fürst, P.; Gundert-Remy, U.; Gürtler, R.; Husøy, T.; Moldeus, P.; Oskarsson, A.; Shah, R.; Waalkens-Berendsen, I.; Wölfle, D.; Benigni, R.; Bolognesi, C.; Chipman, K.; Cordelli, E.; Degen, G.; Marzin, D.; Svendsen, C.; Carfi, M.; Vianello, G.; Mennes, W.; EFSA Panel on Food Additives and Flavourings (FAF). Scientific Opinion on Flavouring Group Evaluation 217 Revision 2 (FGE.217R-ev2), Consideration of Genotoxic Potential for α,β-Unsaturated Ketones and Precursors from Chemical Subgroup 4.1 of FGE.19: Lactones. *EFSA J.* **2019**, *17* (1), No. e05568.

(2) European Commission, Directorate-General for Health and Food Safety. *Commission Regulation (EU) 2019/799 of 17 May 2019 Amending Annex I to Regulation (EC) No 1334/2008 of the European Parliament and of the Council as Regards the Removal from the Union List of the Flavouring Substance Furan-2(5H)-One132*, 2019 http://data.europa.eu/eli/reg/2019/799/oj/eng1214. (accessed June, 2025−06−09).

(3) Dusart, A.; Grosjean, J.; Autuori, M.; Goscinny, S.; Collin, S. Occurrence and Synthesis Pathways of (Suspected) Genotoxic α,β-Unsaturated Carbonyls in Chocolate and Other Commercial Sweet Snacks. *J. Agric. Food Chem.* **2024**, *72* (23), 13308−13319.

(4) Glomb, M. A.; Henning, C. Formation of Reactive Fragmentation Products during the Maillard Degradation of Reducing Sugars − A Review. In *ACS Symposium Series*; Granvogl, M.; Peterson, D.; Schieberle, P., Eds.; American Chemical Society: Washington, DC, 2016; Vol. *1237*, pp 117−131.

(5) Liu, J.; Wan, P.; Xie, C.; Chen, D.-W. Key Aroma-Active Compounds in Brown Sugar and Their Influence on Sweetness. *Food Chem.* **2021**, *345*, No. 128826.

(6) Perez Locas, C.; Yaylayan, V. A. Origin and Mechanistic Pathways of Formation of the Parent FuranA Food Toxicant. *J. Agric. Food Chem.* **2004**, *52* (22), 6830−6836.

(7) Fan, V. K.; Rohn, S.; Kanzler, C. Bildung von C4-Furanonen in Der MAILLARD-Reaktion von Maltose Und L-Lysin. *Lebensmittelchemie* **2021**, *75* (S2), S080.

(8) Liu, S.; Jin, Y.; Huang, S.; Zhu, Q.; Shao, S.; Lam, J. C.-H. One-Pot Redox Cascade Paired Electrosynthesis of Gamma-Butyrolactone from Furoic Acid. *Nat. Commun.* **2024**, *15* (1), No. 1141.

(9) Delatour, T.; Huertas-Pérez, J. F.; Dubois, M.; Theurillat, X.; Desmarchelier, A.; Ernest, M.; Stadler, R. H. Thermal Degradation of 2-Furoic Acid and Furfuryl Alcohol as Pathways in the Formation of Furan and 2-Methylfuran in Food. *Food Chem.* **2020**, *303*, No. 125406.

(10) Schöpf, A.; Oellig, C.; Granvogl, M. Formation of Furanoic Compounds in Model Systems with Saccharides, Amino Acids, and Fatty Acids, Analyzed with Headspace-Solid Phase Micro-Extraction-Gas Chromatography−Tandem Mass Spectrometry. *J. Food Bioact.* **2022**, *20*, 61−71.

(11) Kanzler, C.; Schestkowa, H.; Haase, P. T.; Kroh, L. W. Formation of Reactive Intermediates, Color, and Antioxidant Activity in the Maillard Reaction of Maltose in Comparison to d-Glucose. *J. Agric. Food Chem.* **2017**, *65* (40), 8957−8965.

(12) Hollnagel, A.; Kroh, L. W. 3-Deoxypentosulose: An α-Dicarbonyl Compound Predominating in Nonenzymatic Browning of Oligosaccharides in Aqueous Solution. *J. Agric. Food Chem.* **2002**, *50* (6), 1659−1664.

(13) Vanderhaegen, B.; Neven, H.; Verstrepen, K. J.; Delvaux, F. R.; Verachtert, H.; Derdelinckx, G. Influence of the Brewing Process on Furfuryl Ethyl Ether Formation during Beer Aging. *J. Agric. Food Chem.* **2004**, *52* (22), 6755−6764.

(14) Berg, H. E. Reactions of lactose during heat treatment of milk: a quantitative study, PhD Thesis; Agricultural University: Wageningen, 1993 DOI: 10.18174/203007.
(15) Chiku, K.; Yoshida, M.; Ono, H.; Kitaoka, M. Generation of 3-Deoxypentulose by the Isomerization and β-Elimination of 4-*O*-Substituted Glucose and Fructose. *Carbohydr. Res.* **2021**, *508*, No. 108402.
(16) Mori, M.; Ito, K. Effects of pH on the Formation of Volatile Products in Non-Enzymatic Browning of Maltose. *Food Sci. Technol. Res.* **2004**, *10* (1), 60−64.
(17) Mavric, E.; Henle, T. Isolation and Identification of 3,4-Dideoxypentosulose as Specific Degradation Product of Oligosaccharides with 1,4-Glycosidic Linkages. *Eur. Food Res. Technol.* **2006**, *223* (6), 803−810.
(18) Brands, C. M. J.; Van Boekel, M. A. J. S. Reactions of Monosaccharides during Heating of Sugar−Casein Systems: Building of a Reaction Network Model. *J. Agric. Food Chem.* **2001**, *49* (10), 4667−4675.
(19) Troyano, E.; Olano, A.; Jimeno, M. L.; Sanz, J.; Martínez-Castro, I. Isolation and Characterization of 3-Deoxypentulose and Its Determination in Heated Milk. *J. Dairy Res.* **1992**, *59* (4), 507−515.
(20) Huang, H.; Chen, J.; Zheng, M.; Zhang, L.; Ji, H.; Cao, H.; Dai, F.; Wang, L. Precursors and Formation Pathways of Furfural in Sugarcane Juice during Thermal Treatment. *Food Chem.* **2023**, *402*, No. 134318.
(21) Limacher, A.; Kerler, J.; Davidek, T.; Schmalzried, F.; Blank, I. Formation of Furan and Methylfuran from Ascorbic Acid in Model Systems and Food. *J. Agric. Food Chem.* **2008**, *56* (10), 3639−3647.
(22) Wnorowski, A.; Yaylayan, V. A. Influence of Pyrolytic and Aqueous-Phase Reactions on the Mechanism of Formation of Maillard Products. *J. Agric. Food Chem.* **2000**, *48* (8), 3549−3554.
(23) Kanzler, C.; Schestkowa, H.; Haase, P. T.; Kroh, L. W. Formation of Reactive intermediates, Color, and Antioxidant Activity in the Maillard Reaction of Maltose in Comparison to D-Glucose. *J. Agric. Food Chem.* **2017**, *65* (40), 8957−8965.
(24) Schöpf, A.; Steliopoulos, P.; Oellig, C. Formation of Furan and Furan Derivatives in Baby Food Products. *Food Chem.* **2025**, *464*, No. 141557.
(25) Albouchi, A.; Murkovic, M. Formation Kinetics of Furfuryl Alcohol in a Coffee Model System. *Food Chem.* **2018**, *243*, 91−95.
(26) Wherry, B. M.; Jo, Y.; Drake, M. A. Concentration of Furfuryl Alcohol in Fluid Milk, Dried Dairy Ingredients, and Cultured Dairy Products. *J. Dairy Sci.* **2019**, *102* (5), 3868−3878.
(27) Birlouez-Aragon, I.; Moreaux, V.; Nicolas, M.; Ducauze, C. J. Effect of Iron and Lactose Supplementation of Milk on the Maillard Reaction and Tryptophan Content. *Food Addit. Contam.* **1997**, *14* (4), 381−388.
(28) Verduci, E.; Di Profio, E.; Corsello, A.; Scatigno, L.; Fiore, G.; Boseti, A.; Zuccotti, G. V. Which Milk during the Second Year of Life: A Personalized Choice for a Healthy Future? *Nutrients* **2021**, *13* (10), No. 3412.
(29) Brereton, K. R.; Green, D. B. Isolation of Saccharides in Dairy and Soy Products by Solid-Phase Extraction Coupled with Analysis by Ligand-Exchange Chromatography. *Talanta* **2012**, *100*, 384−390.
(30) Patton, S. Studies of Heated Milk III. Mode of Formation of Certain Furan Compounds. *J. Dairy Sci.* **1950**, *33* (12), 904−910.
(31) Krause, S.; Keller, S.; Hashemi, A.; Descharles, N.; Bonazzi, C.; Rega, B. From Flours to Cakes: Reactivity Potential of Pulse Ingredients to Generate Volatile Compounds Impacting the Quality of Processed Foods. *Food Chem.* **2022**, *371*, No. 131379.

https://doi.org/10.1021/acsfoodscitech.6c00226
ACS Food Sci. Technol. XXXX, XXX, XXX−XXX